SUPPLEMENT: INDEX TO VOLUME 188

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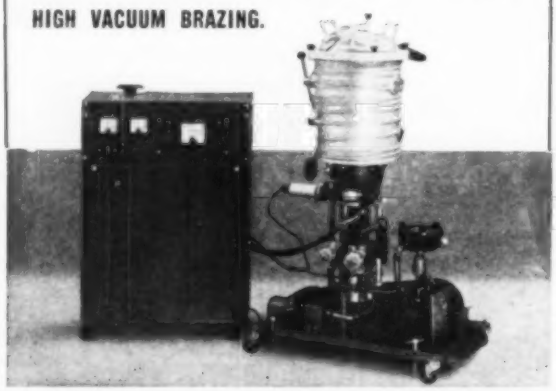

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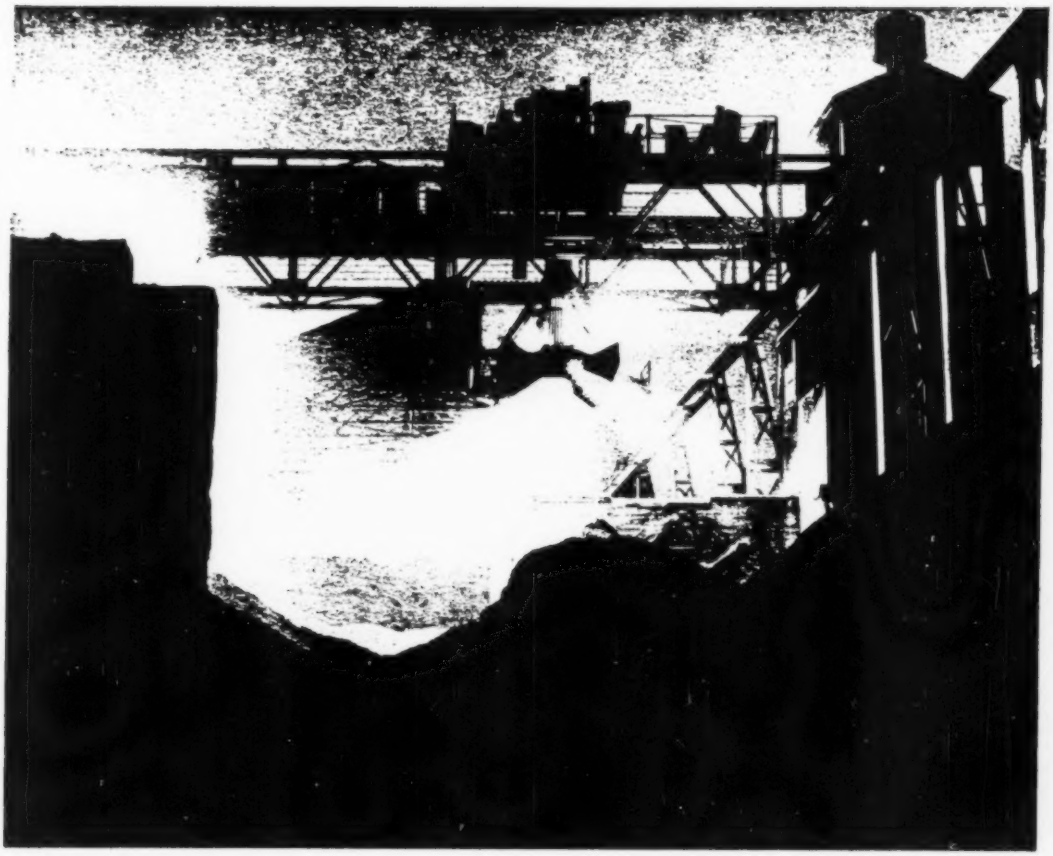

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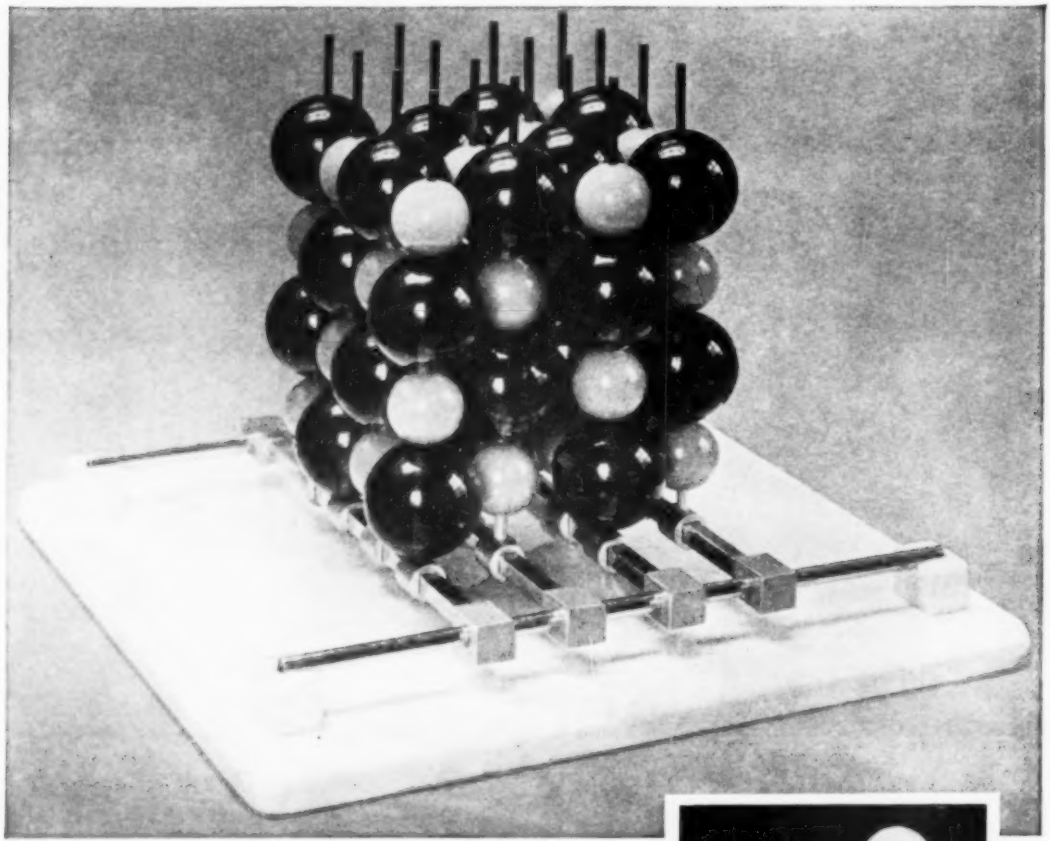

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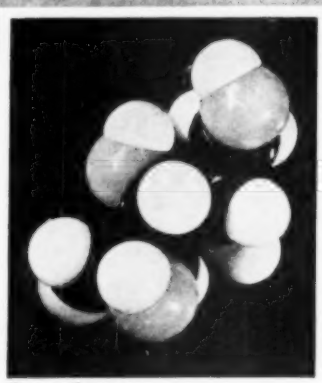

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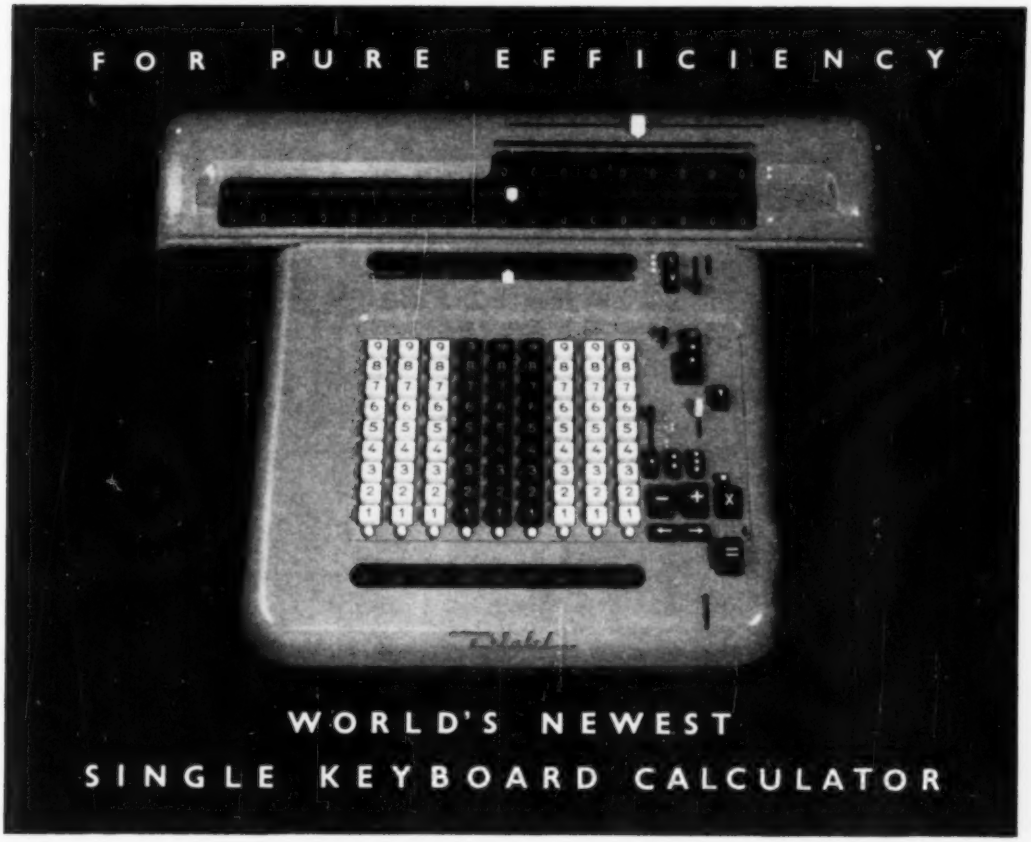

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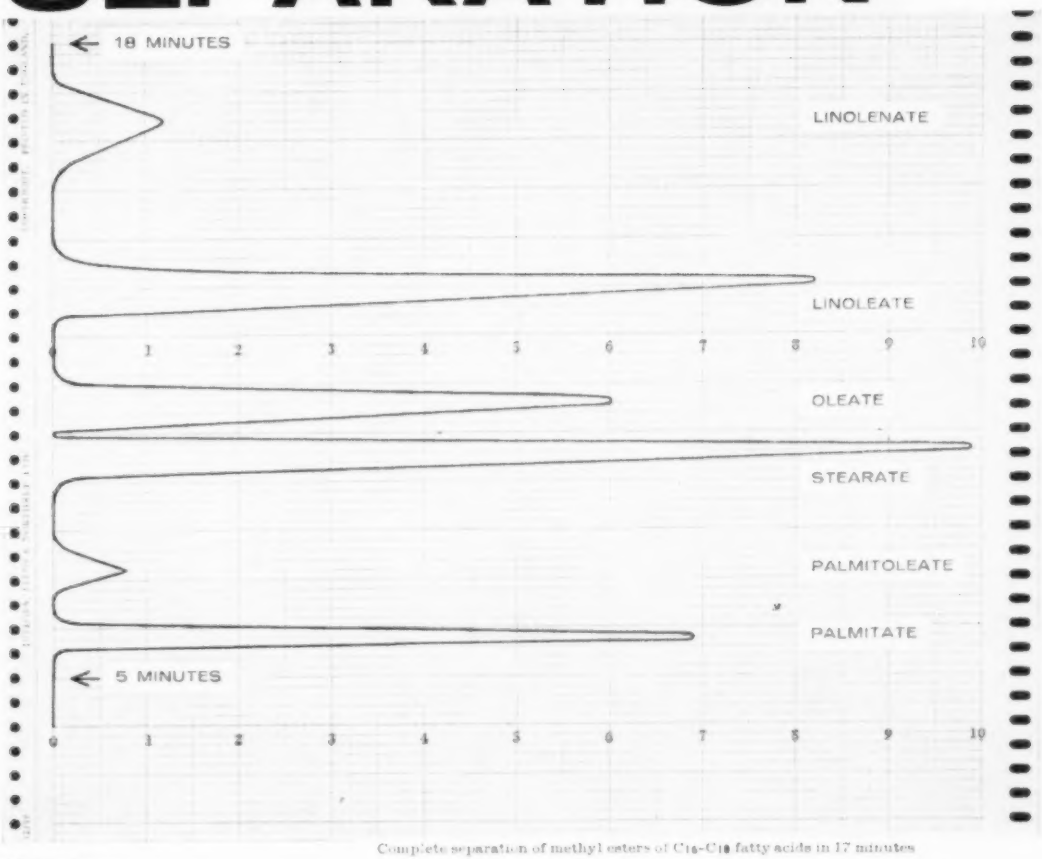

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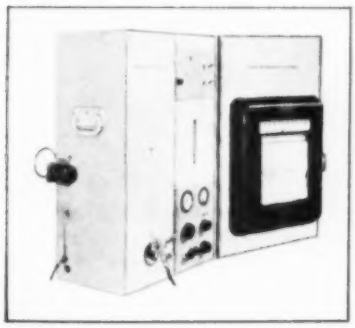

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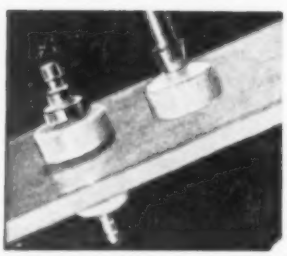

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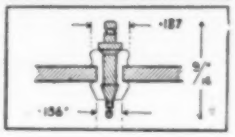

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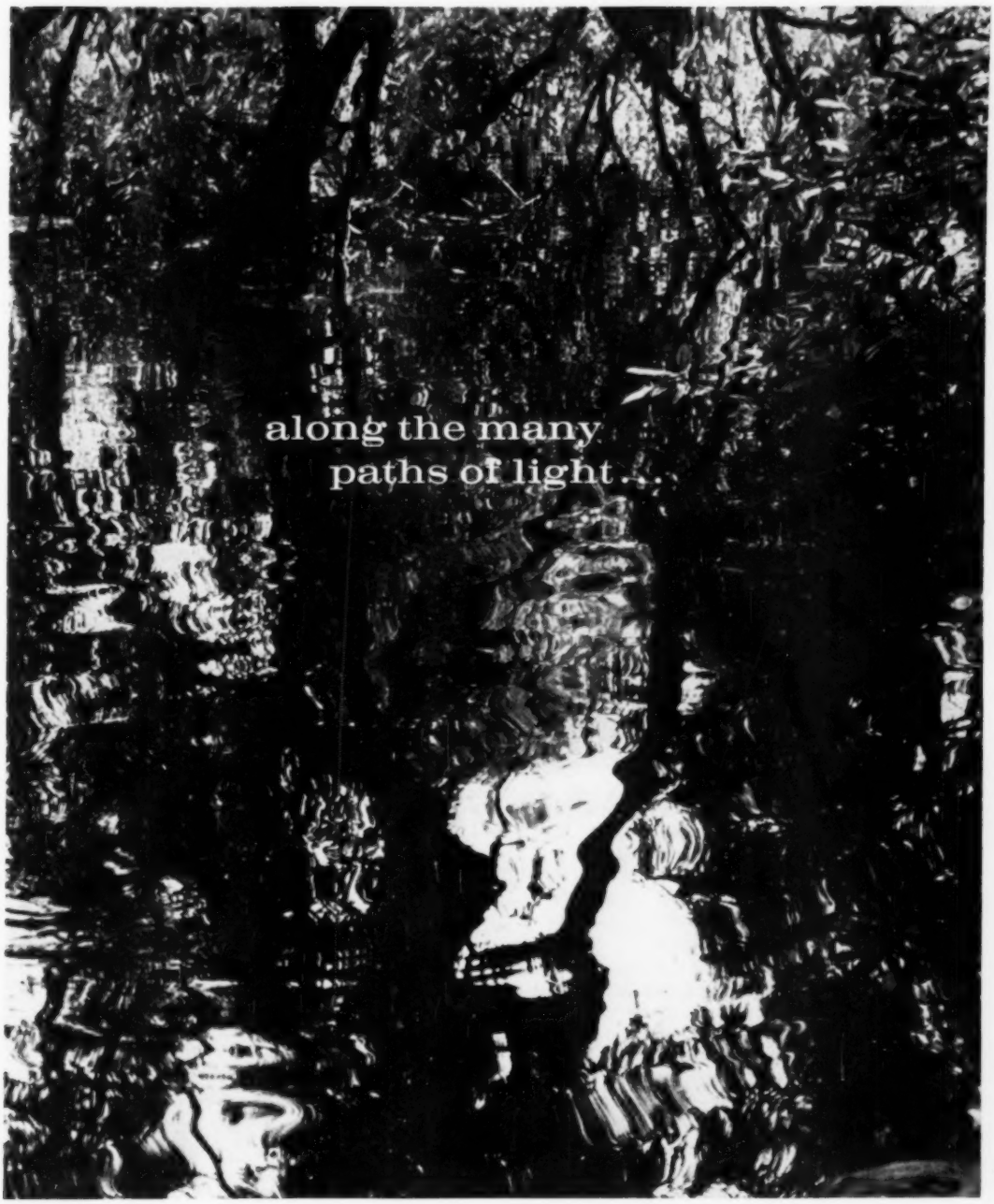

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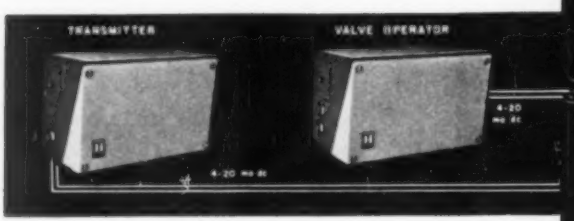

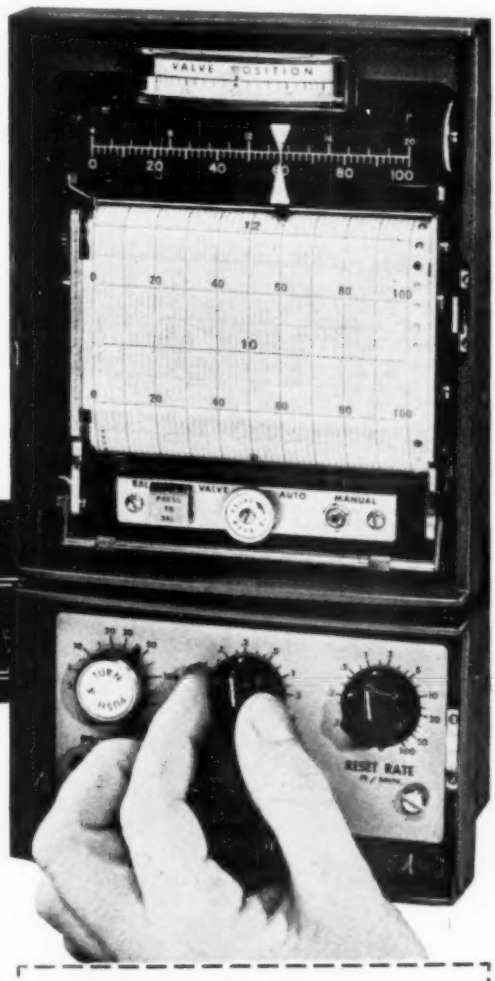

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CONTENTS

	Page
Science and the Humanities	695
Plant Morphogenesis. By Prof. C. W. Wardlaw	697
Modern Armamentarium of Therapeutics. By Prof. F. Bergel, F.R.S.	699
Birds and Men in Borneo. By Dr. L. Harrison Matthews, F.R.S.	699
Vegetation and Forest Trees of Ghana. By Dr. E. W. Jones	700
The Convolution Transform. By Prof. T. A. A. Broadbent	700
Better Opportunities in Technical Education. By Dr. P. F. R. Venables	701
Golden Jubilee of the Biochemical Society. By Dr. P. M. Campbell and Dr. W. J. Whelan	702
Gene Evolution and the Hæmoglobins. By Prof. Vernon M. Ingram	704
Obituary: Prof. J. T. Patterson. By Prof. M. J. D. White	709
News and Views	710
Recent Developments in Plant Nematology. By Dr. J. B. Goodey	715
Area of Residence of Mental Hospital Patients	716
Community Mental Health	717
The Hydrocharitaceæ in New Zealand	718
Choice of Tree Species. By Prof. M. L. Anderson	719
Energy-linked Cytochrome Oxidation in Mitochondria. By Prof. Britton Chance	719
Submolecular Structure of the Nucleic Acids. By Prof. Bernard Pullman and Alberte Pullman	725
Detection of Liver Proteins in Circulating Blood. By Dr. A. H. Gordon	727
Affinity of Organic Compounds for Free Electrons with Thermal Energy: its Possible Significance in Biology. By Dr. J. E. Lovelock	729
Aggregation, Variance and the Mean. By L. R. Taylor	732
Surface Orientation and Friction of Graphite, Graphitic Carbon and Non-Graphitic Carbon. By Dr. J. W. Midgley and D. G. Teer	735

(Continued overleaf)

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LETTERS TO THE EDITORS

ASTROPHYSICS — Page

Rotation Period of the Artificial Satellite 1958δ1.—P. Notni and H. Oleak; C. R. Faulkner . 737

HD 101065—a *G0* Star with High Metal Content.—Dr. Antoni Przybylski 739

The Total Electron Content of the Ionosphere during the Magnetic Disturbance of November 12–13, 1960.—G. N. Taylor 740

PHYSICS

Optical Demonstration of Bragg's Law.—Prof. W. G. Burgers 741

Acceleration of Deuterons in a Synchrotron.—H. R. Shaylor and Dr. P. D. Whitaker . . . 741

The Quasi-Longitudinal Approximation to the Appleton–Hartree Equation.—A. D. M. Walker 742

MINERALOGY

Kilchoanite, a Polymorph of Rankinite.—Dr. S. O. Agrell and Dr. P. Gay 743

CRYSTALLOGRAPHY

Etch Patterns on Cadmium Crystals grown from Vapour.—Joy George 743

GEOLOGY

Palæoecology of Carboniferous Peat Bogs.—A. H. V. Smith 744

CHEMISTRY

Polymers and the Theory of Numbers: Molecular Weight Distributions from Rheological Measurements.—E. Menefee and W. L. Peticolas . 745

The BH_4^- Ion in the Lithium Borohydride Lattice.—C. J. H. Schutte 745

Isolation of D-Glycero-D-galacto-heptitol from the Wound Exudate of Avocado Trees.—J. K. N. Jones and R. A. Wall 746

Monosaccharide Sequence in *Pneumococcus* Type XIV Polysaccharide.—Dr. S. A. Barker, M. C. Keith and Prof. M. Stacey, F.R.S. . . 746

BIOCHEMISTRY

Role of Tocopherol, Selenium and Anti-oxidants in the Rat.—E. E. Edwin, J. Bunyan, A. T. Diplock and J. Green 747

Role of Selenium in Relation to Ubiquinone in the Rat.—J. Green, E. E. Edwin, A. T. Diplock and J. Bunyan 748

Tocopherol, Ubiquinones and Ubichromenols in Yeasts and Mushrooms.—A. T. Diplock, J. Green, E. E. Edwin and J. Bunyan . . 749

An Unidentified Ubichromenol-like Lipid Constituent of Bakers' Yeast.—E. E. Edwin, J. Green, A. T. Diplock and J. Bunyan . . 750

Electrophoretic Behaviour of Rat Serum Amylase.—Prof. Robert L. McGeachin and Betty Ann Potter 751

Identification of 3,4,5-Trimethoxyphenylacetic Acid as the Major Metabolite of Mescaline in the Dog.—Prof. Elliot Spector 751

Method of dissolving Triacetyl-oleandomycin for the Assay of Sensitivity of Micro-organisms.—Dr. J. W. Czekalowski 752

Crystalline α-Kojibiose.—Fumio Yamauchi and Kiyoshi Aso 753

PHYSIOLOGY

Plastic Changes of Spinal Monosynaptic Responses from Tenotomized Muscles in Cats.—Dr. W. Kozak and Dr. R. A. Westerman . . . 753

Role of Biliary Alkaline Phosphatase in the Guinea Pig.—Freda Brown (*née* Bowyer) . 755

Alkaline Phosphatase in Cell Cultures of Human Origin.—Dr. Harold M. Nitowsky and Dr. Fritz Herz 756

Prevention of Vagotomy of Erythrocytosis induced by Hypoxæmia.—Dr. D. F. J. Halmagyi and H. J. H. Colebatch 757

Relationship of the Sarcoplasmic Reticulum to Sarcolemma in Sheep Cardiac Muscle.—F. O. Simpson and S. J. Oertelis 758

Partition of Calcium and Phosphorus Excretion in the Laying Hen.—S. Hurwitz and Prof. P. Griminger 759

RADIOBIOLOGY

Protective Action of Calcium Gluconate against After-effects of X-irradiation on Conidia of *Neurospora crassa*.—Prof. J. Weijer . . 760

Protective Effects of Diisopropylfluorophosphonate against the Lethal Effects of X-rays before or after Irradiation.—D. A. Willoughby . 761

Differential Radiosensitivity in Rice (*Oryza sativa* Linn.) at the Genotypic Level.—H. K. Shama Rao and K. C. Bora 762

Metabolism of Carboxyl-^{14}C-labelled 2,4-Dichlorophenoxyacetic Acid by Bean Stems: Heterogeneity of the Ethanol-soluble, Ether-insoluble Products.—Michael K. Bach and J. Fellig 763

Excretion and Hepatic Storage of 5,6-Dimethylbenziminazolyl Cobamide Coenzyme labelled with Cobalt-58.—Wolmar Nyberg, Matti Saarni and Dr. Ralph Grässbeck 764

HÆMATOLOGY

Occurrence of Heparin in the Blood of Fish and its Prevention of the Clotting of Fish Plasma.—Dr. S. Z. Qasim and R. Hasan . . . 764

A New Hæmoprotein with a Unique Iron Porphyrin Prosthetic Group isolated from Human Erythrocytes.—Dr. Martin Morrison . . 765

HISTOLOGY

Mast Cells in Peripheral Nerve Trunks.—H. J. Gamble and Prof. Stephen Goldby . . . 766

PATHOLOGY

Histochemical Evidence of 5-Hydroxytryptamine in a Dog Mast Cell Tumour.—Prof. W. G. Rice and Dr. James Mitchener 767

Identification of So-called Atypical Macroglobulinæmia as an Atypical Form of β_{2A}-Paraproteinæmia: a New Immunological Entity?—R. E. Ballieux, Dr. J. W. Imhof and G. H. Nichaus 768

Fibrosarcoma in a Rabbit following β-Irradiation of the Skin.—L. A. George, S. Marks and L. K. Bustad 770

BIOLOGY

Promotion of Leaf Growth by Short Days in the Short-Day Plant *Chenopodium amaranticolor*.—Roderick G. Thomas 771

Estimation of Oil in Safflower Seed.—S. H. Pawlowski 772

Potato Root Eelworm in the Canary Islands.—R. Chamberlain 773

A Technique for Destruction of the Pineal Body using Yttrium-90 Spheres.—Dr. Uno Holmgren and Dr. Gustaf Notter 773

A Biennial Copepod from Lake Hazen, Ellesmere Island.—Dr. I. A. McLaren 774

BACTERIOLOGY

Biosynthesis of Acetoin by *Leuconostoc citrovorum*.—M. Busse and Prof. O. Kandler . . . 774

Chloramphenicol, a Simultaneous Carbon and Nitrogen Source for a *Streptomyces* sp. from Egyptian Soil.—Prof. Y. Abd-el-Malek, M. Monib and A. Hazem 775

PSYCHOLOGY

An Unexpected Effect of Attention in Peripheral Vision.—B. Babington Smith 776

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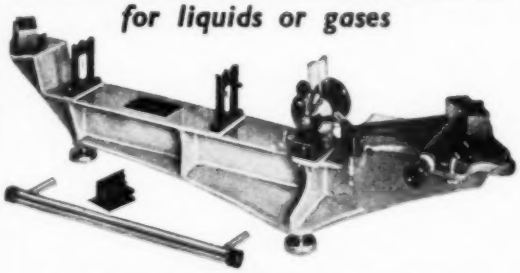

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SCIENCE AND THE HUMANITIES

JUST over a century ago, J. S. Mill, in his famous essay on liberty, remarked that "the general tendency of things throughout the world is to render mediocrity the ascendant power among mankind". He added that there is always a need for persons not only to discover new truths and point out when what were once truths are true no longer but also to commence new practices, and set the example of more enlightened conduct, and better taste and sense in human life. All that is still profoundly true to-day, and in fact the advent of the mass media of communication has accentuated the danger of mediocrity or worse. Those passages could well have been in the mind of Dr. Caryl Haskins in writing his report for 1959–60 as president of the Carnegie Institution of Washington*, which once again gives a percipient and imaginative survey of the inter-relations of the scientific disciplines with themselves and with the society in which they are nurtured.

While the present report follows closely on last year's report and develops further the same lines of thought then advanced, particularly those arising out of consideration of a real or imagined dichotomy between the scientific and non-scientific world, such as Sir Charles Snow discussed in his Rede Lecture, "The Two Cultures", it is nevertheless fully independent. In her recent life of Lord Lugard, in writing of Lady Lugard, Dr. M. Perham observes: "Even to-day . . . the exceptional and independent mind can often be traced to some divergence from the usual course of schooling which has given both stimulus to thought and freedom to read at will". Although Dr. Haskins's address can scarcely be described as an exposition of this text, it is clear enough that he is profoundly disturbed at some educational tendencies to-day, and that he places very high among his presidential responsibilities that of fostering the exceptional and independent mind, and giving such minds every opportunity to render the contributions to scientific and technological advance which they alone can make.

Dr. Haskins begins by emphasizing the vistas of insight and wonder inconceivable to our forefathers, which we enjoy because of the unparalleled advances in our appreciation and comprehension of Nature, and suggesting that, in consequence, this generation may be standing at a major cross-road of history and living in that deep travail which more than once has preceded and ushered in a Golden Age. The brilliance and variety of man's concepts to-day, the diversity of his imagination, the extent of his practical power to shape and to use his material environment, perhaps even the penetration of his understanding, have never been remotely rivalled in all earlier history, nor have the dangers of his very existence seemed as vivid, as omnipresent, as remote from resolution. While we are convinced that the values in which our society is rooted are fundamental to us, yet we are constantly haunted by the feeling—and the evidence—that the means by which we have traditionally implemented and expressed them in the past, if projected into the coming years without innovation and imagination, will be inadequate to our future.

What is less obvious is the challenge that this contrast presents, and Dr. Haskins reminds us that the great ages of mankind, the ages of the most radical changes and the biggest advances, the ages that later generations of men called great, were not the times of easy optimism when man thought everything discovered, everything designed, everything finished. As Whitehead wrote, on the whole the great ages have been unstable ages. Greatness and ease, vast innovation and untroubled stability, are no more compatible among nations or in a world community than they are among individuals. To-day the United States is predominantly a scientific and technical nation, living in an age itself characterized by the explosive development of science throughout the world, and Dr. Haskins asks accordingly whether there may not be significant things which the very structure of science as a way of life could say in aid of the understanding of ourselves, of this age and the task of the American nation—of an age and a nation profoundly shaped by science at a secular level and at a deeper and more spiritual level too.

That question could well be addressed to Britain also, and the answer we give to it should determine very largely the answers to be given to many of the questions now arising in regard to the expansion of university and technological education, of specialization in the sixth forms of schools and elsewhere, and of the nature and extent of general education. Dr. Haskins develops his theme with imaginative insight to show how in the growth of modern science from the time of Leonardo da Vinci it has been sensitively responsive to the moods and needs of men, portraying accurately the successive ages which nourished it. Everywhere it took its character from the conspicuous needs and opportunities of the time, developing greatness in those areas where it was most needed; and in turn its spirit was everywhere reflected in the society that it served. Surely it is not accidental, he argues, that the centuries of the flowering of modern science have also been the centuries of the rise of the Western concept of the dignity, the uniqueness, and the essential worth of the individual, or that these were also the centuries of the genesis and ascendency of the modern Nation-State as we understand the term to-day.

While in these four centuries there have been comparatively static or satisfied interludes, the main trends in science have been marked by instability, vast shifts in man's concepts of his universe and his

* Carnegie Institution of Washington. The Report of the President, 1959–1960. Pp. xiii–lxxiv. (Reprinted from *Carnegie Institution of Washington Year Book*, 59.) (Washington, D.C.: Carnegie Institution of Washington, 1960.)

place in it, and of his own very constitution and nature, delight in ideas, or fascination with them because of their compelling sweep and force, and an overwhelming urge to communicate them broadly and to share widely in them. The ages that have witnessed these trends have been characterized, too, by the attainment of new levels of physical well-being and of the moral and spiritual horizons and opportunities of the individual. Simultaneously have come, both as cause and consequence of these developments, demands for innovation in the structure of society, reflected in social and political insecurity and in rapidly shifting patterns of political and social organization. The more we contemplate our own time, the more it seems to resemble those earlier dynamic and critical eras of Western history, typically characterized by a keen sense of change and exploration and also by an atmosphere of personal, political and social insecurity. The eagerness with which developments in the exploration of space are watched is only an illustration of the sense of new physical frontiers close at hand, the ferment of new ideas and the vast shifts in the individual's notion of the universe and his place in it, of his very nature, that mark our time like those of Leonardo, Columbus, Magellan and Vasco de Gama. There are the same new and violent and little-understood demands of political and social organization and the same intense need for vigorous and imaginative leadership in every field.

Dr. Haskins does not omit to point out that some of the changes with which we are concerned so vastly exceed those that occupied other ages as almost to differ in kind. The magnitude and variety of our sources of power, the capacity for essentially instantaneous communication have, for example, forced a major human adjustment on the West before it would accustom itself to this range and speed of communication, and new nations are called to make the same great orientation in a world which allows little time for major re-adjustments of international affairs. Further, new levels of human integration are demanded by the very pressure of population and the intricacy of modern life, and with the control, modulation and organization of the new sources of physical power calling for particular attention, an order of leadership and of excellence in every sphere greater than we have yet known is also demanded—a leadership of greater force, greater knowledge, greater understanding, and one more widely dispersed in every level of our society.

Here, in touching on science and leadership, Dr. Haskins is concerned, not so much with the leadership of science itself, as in relation to the position of science within the framework of the character, the aspirations, and the contemporary needs of a nation, particularly the United States. He stresses the value placed on individual excellence, the dependence of the essential worth of life for the individual in a dedication larger than himself, and the way in which such total dedication spans the work-day world no less than the religious realms. Reasoning thus, the supreme importance which science attaches to the individual leads him to regard science as one of the spiritual factors in a democracy, closely resembling in its own society that of a democracy, deeply motivated by an ethic at once basically religious in character and dedicated both to the supremacy of the individual and to that spirit of frontier uncomformity which is a pronounced and precious element in the American tradition.

Science, then, is one of the most precious spiritual and moral, as well as material, values in our society, and it serves us to-day in a particularly critical time, and nowhere more so than in its emphasis on the individual. Originality and independence, individual dissent, properly protected, are the very essence of our civilization; and for science in its public function, the protection of the individual and his independence, the honour of free thought and free expression and the public welcome of dissent are all vital. To-day, however, they are threatened, not so much by formal oppression or suppression, or organized intolerance, as by more subtle and insidious factors—inattention, lassitude, hostility to innovation through misunderstanding of its nature and effect, especially the threat of simple, widespread, massive misunderstanding of the nature of the scientific way, its purpose and its indispensable place and part in our practical world and in our deepest philosophy and belief.

At this point Dr. Haskins returns to the analysis of the apparent dichotomy of the two cultures on which he touched in his previous presidential report, and, like Sir Cyril Hinshelwood, he regards the common factors that unite all the creative disciplines, be they artistic or humanistic, philosophical or scientific, as far deeper and more fundamental than the more obvious differences that distinguish them. Pointing out that in the earlier days of scientific effort, before the sheer weight of learning and evidence forced our modern specialization, many great figures frequently united the two fields, he stresses the essential identity, at their most general level, of the characteristics and objectives of the arts and of the sciences. Both are primarily concerned with the process of discovery itself, and with discerning the beauties of Nature. Both professionally excel in innovation, and take delight in the shapes of things, their patterns, lights and shades, and in the uncovering of hitherto unperceived relations. Both seek to cast their descriptions and discoveries in evocative and universal forms, and at a very profound level of understanding; both take communicability and coherence, within the subject itself and with the audience, as the ultimate criterion of conceptual or of demonstrated truth. Nor is this all. Both take their very living being and draw their vitality from the joy of discovery, from the attaining of ends unknown when the work was begun, through means which are indeed partly or wholly unknown, but usually of technical difficulty. Both are deeply concerned with the underlying likeness between superficially unlike things; with the equating of different

aspects of the same phenomena; with uniting such apparently disparate aspects in common matrices; with the generalizations which follow painstakingly minute analyses, with analogies and their testing. Typical of all the most creative and imaginative pursuits of man, of the life processes themselves, the arts and the humanities, quite as much as the natural sciences, must be truly consonant with our contemporary history; and as faithfully as they reflect their period, so they are reinforced by the societies that nourish them.

There are, of course, important differences between the disciplines of the arts and the humanities existing at another level, and these too must be fully recognized and understood. Dr. Haskins's penetrating analysis is particularly valuable here, and he does not suggest that it will be easy to heal the rifts that have grown between the kingdoms of the humanities and the natural sciences, between the bodies of thought that they comprehend and the men who are their practitioners. That the fundamental similarities, the bonds of common purpose and of common tasks unite them more strongly and more deeply than these differences are plain to see; and they offer foundations on which to build, to bridge the gaps of understanding and of sympathy, to undo the damage and eliminate potential dangers that arise. But this will not be the easier because the rifts should not exist.

First, Dr. Haskins suggests, in art coherence is primarily internal, uniting the parts of one creation. In the natural sciences, however, it is in a sense external, at its best uniting in one theoretically coherent frame the fruits of many thinkers, whose work is often extremely disparate in character. Again, in art communication and communicability extend primarily between the creator of the work and his audience, at once his witness and his critic, and such communication comes primarily after the work itself is finished. In science, on the other hand, communication is at least as active during the progress of the work as after its completion, and in a very deep sense science is fundamentally a communal activity. Though the steps of innovation lie most often with the individual, truth for science more than ever before inheres in a composite fabric of evidence and interpretation, derived from a great body of communicating investigators examining Nature from a multitude of points of view.

Truth in our day, Dr. Haskins maintains, is a property of this common fabric of accepted knowledge shared among all the working scientists in a given field, and it is for this reason that the scientific community is in essence a world community, transcending the boundaries of nations. There is probably no close counterpart to this aspect of the scientific effort within the arts; but on the other hand, while in the arts imagination alone may fix the final limits of shared experience, in science, despite the indispensable assistance given by imagination in discerning those limits and in reaching the goals they define, the limits themselves are determined by the concrete evidences of verification and therefore, ultimately, of the human senses. Nevertheless, Dr. Haskins does not omit to point out that this ultimate criterion is itself relative, joining the observer and his environment in a system from which he can never be isolated.

From this communal characteristic of science many striking contrasts between its operating modes and those of the arts are derived. One is the strong tendency to specialize, which is so characteristic of the natural sciences to-day. Dr. Haskins recognizes that specialization is essential to scientific progress; but he has wise words about the dangers which attend the consequent fragmentation of science and the need to deal adequately with the problem of communication in order that the rich opportunities which are offered by the borderlands of two or more disciplines may be explored and seized.

In this presidential report, Dr. Haskins thus ranges imaginatively and suggestively over a wide field, recognizing alike the intellectual and spiritual value of science for its own sake, its suggestive affinities with and differences from the arts and humanities, and its pragmatic importance as the architect of great material power. His review is notable for the dignity as well as the range of its thought. Dr. Haskins recognizes that it is imperative that we understand the nature and the needs of the scientific way, and comprehend the dangers that may menace it; and his review is commended to the attention of all concerned with the organization of Britain's scientific effort or the shaping of her educational institutions to meet the needs of to-day and to-morrow. They will indeed find here no blue-prints or prescriptions for policy, but they may gather some penetrating insights to the nature and needs of our larger society, some vision to inspire the leadership needed in a critical period of history the challenge of which for the future may well be, as Dr. Haskins suggests, without parallel in human experience.

PLANT MORPHOGENESIS

Plant Morphogenesis

By Prof. Edmund W. Sinnott. (McGraw-Hill Publications in the Botanical Sciences.) Pp. x+550. (New York: McGraw-Hill Book Company, Inc.; London: McGraw-Hill Publishing Company, Ltd., 1960.) 97*s*.

DURING the past twenty years, a not inconsiderable number of books and reports of symposia have been concerned with morphogenesis in plants, either from some particular point of view or in its more general aspects. The subject is in no sense new, though at different times it has been described by different names. During the nineteenth century, Naegeli, Hofmeister, Sachs, Vöchting and many others were deeply involved in the problems of the inception and development of form and structure in plants; and the present century has had some notable exponents of the subject, which now has many adherents. Yet there is justice in Prof. Sinnott's statement that few, if any, attempts have been made

to treat the subject as a whole and that no extensive synthesis of its content has been undertaken. Now, after forty years as a research worker in this field, he has written the book under review—assuredly a gigantic and formidable undertaking. From the outset it is evident that he is fully aware that, in attempting a comprehensive treatment of this large subject, he is unlikely to please all his readers and that, at every point, he lays himself open to the criticisms of those with special knowledge of some particular aspect. Nevertheless, works of synthesis must be attempted by those who possess the necessary outlook, knowledge and courage, if botanical science is to retain some semblance of coherence. For this reason alone, Prof. Sinnott's book seems likely to have an important impact on botanical science.

The author has set about his task by introducing some idea of what is involved in morphogenesis, rightly emphasizing the importance of the central, if enigmatic, concept of biological organization; for at every developmental level at which there is visible expression of organic form there is evidence of unity and harmony of development, indicating the existence of co-ordinations and other inner relationships in which both genetical and extrinsic factors are involved. Part 1 of the book then begins with a consideration of growth in general, its cellular basis, and the histological constitution of apical and other meristems. In this section, also, the author has dealt, adequately and lucidly, though rather briefly, with experimental studies which have contributed to our understanding of the constitution and morphogenetic function of apical meristems. In view of the wealth of interesting illustration of apical meristems, contributed by investigators all over the world, it seems a pity, especially for student readers, that this section is so scantily illustrated.

In Part 2, the author has considered the phenomena of morphogenesis, dealing with such topics as correlation, polarity, symmetry (including the phenomena of phyllotaxis), differentiation, regeneration, chimæras and abnormal growth. This section, in short, relates to much that has been of acute interest to physiologists and others over many decades, but particularly during the more recent period. For the general botanist, and for the student of morphogenesis in particular, this section contains much fascinating and well-documented information, set forth in a simple and readable fashion.

In Part 3, the numerous and diverse factors in morphogenesis are considered, including light, water relationships, temperature, other physical factors, chemical factors in general and growth substances in particular, and of course, genetical factors. It is in this section, where a vast amount of specialized information, of very different kinds, has had to be considered and compressed into a relatively small number of pages, that the author is probably most vulnerable. He has, indeed, undertaken a task which, in view of the contemporary output of botanical research, is more appropriate to a team than to an individual. Nevertheless, he has made available to the reader a general survey of many of the factors that are involved in morphogenetic processes, and he has constantly reminded him that these factors never work in isolation: on the contrary, it is to their interaction that many of the distinctive features of living entities must be attributed.

The final chapter of the book deals with organization, obviously a topic of paramount importance in biology, but one on which few botanists have attempted to put pen to paper. However elusive and enigmatic this concept may be, its importance cannot be over-estimated. After all, some attempt to understand what constitutes organization is implicit in the aims and outlook of all those who undertake serious investigations of morphogenesis. In this chapter, which is the essence and summation of his book, Prof. Sinnott recognizes that several morphogenetic 'components' are of very wide occurrence in the plant kingdom and contribute fundamentally to the general phenomenon of organization. These components—polarity, differential gradients, symmetry and spirality—are also described as "inherent or basic tendencies". They "seem to be distinct characteristics and may have different bases in protoplasm. . . . All of them, or their rudiments, seem to be present in all plants. They provide the basic ingredients, so to speak, out of which the developmental norm is produced. Just what a specific norm will be depends on the interaction between these inherent protoplasmic traits and two other factors: the genetic constitution of the individual and the environment in which it develops". The genes, in a particular environment, act on these protoplasmic traits to produce the specific form of the organism. But, as the author points out, how genes control developmental relationships, and thus the production of organic form, is unexplored.

The author also discusses what gives unity and self-regulatory character to an organism, and concludes that ontogenetic unity, and also regenerative developments, are not so much due to the unchanging genetic constitution but to the "developmental norm, immanent in the organism from the first and often reached over different routes". In brief, the elucidation of self-regulatory, 'normative development' is regarded as the central problem in the phenomenon of organization. The difficulty of the task is indicated by the numerous workers, cited by the author, who have ventured into this field of inquiry. A synthesis of evidence from many different sources is, of course, essential, but what will come out of the attempted synthesis will, in the author's view, largely depend on the attitude and philosophic outlook of the investigator. After discussing some of the more interesting and relevant ideas that have been proposed to account for biological organization, Prof. Sinnott concludes quite simply by saying that, after all, we still have no idea of what the underlying physical basis really is. But, as is proper to one who has undertaken such an onerous task as the present book, he is not unhopeful, though he recognizes that the phenomenon of self-regulatory organization may well involve principles as yet undiscovered. These may prove to be distinctively biological and different from those at present available from the physical sciences—a conclusion which is not unlike that of some other contemporary exponents. This is a stimulating chapter, and although much of the ground that it covers is not new, it is, nevertheless, individualistic and provocative and is likely to create much new interest and discussion.

In an extensive work such as this it would be surprising if there were not grounds for criticism, of factual detail, emphasis, treatment, and so on. Some readers will no doubt find the text somewhat thin in places, for example, the treatment of embryo-

genesis. In the present review it is not necessary to enter into a discussion of such details. But there can be no doubt that Prof. Sinnott has produced an important and impressive book, one which seems likely to stimulate and hold its place in university teaching and research for many years to come.

C. W. WARDLAW

MODERN ARMAMENTARIUM OF THERAPEUTICS

Medicinal Chemistry

Edited by Prof. Alfred Burger. Second edition. Pp. xiii+1243. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 280s.

IT is the usual procedure that second editions of successful books are corrected versions of the original opus, with certain parts brought up to date. Prof. Alfred Burger must have faced a difficult decision when changing his role from that of solo author of the first edition to that of editor-in-chief and part-author of the new volume, at the same time re-organizing its contents. With due regard to his achievement as represented by the older version, it was a wise decision—because he has assembled around him an impressive list of contributors, holding industrial as well as academic or Government positions, but still reserving for himself the lion's share. The choice of one instead of two volumes is perhaps less fortunate as the weight of the present tome prevents one from reading certain chapters with leisure after working hours. It is also a matter for slight criticism that he selected an all-American team, which, in spite of the high standing of the individual scientists, diminishes somewhat the threads of international connexions so closely interwoven with successful research.

That does not mean that the writers on various aspects of medicinal chemistry (which, as Burger points out, can be equated with pharmaceutical chemistry and represents one very important chapter of applied organic chemistry plus pharmacology, experimental pathology and microbiology, etc.) have neglected results not originating with efforts in the United States. But with the best of intentions for fair play, a certain 'parochial' note creeps in sometimes, the reference to proprietary names, to major illnesses and pharmaceutical sales, to cholinergic instead of parasympathomimetics and to adrenergic instead of sympathomimetic drugs (Dale clearly reserved the expressions 'cholinergic' and 'adrenergic' for structures and nerves of the autonomic system). It should be said that only a very close study of the book discloses these relatively unimportant shortcomings; the overall impression is favourable, with the consequence that this volume will acquire many friends in many countries.

If a few suggestions for the third edition may be added, these are examples: an overall division into symptomatic, etiotropic (chemotherapeutic) remedies and drugs for restitutional therapy could have been given as a table and used as chapter-grouping; the historical table (2-11) has a few omissions, for example, Kennaway's name against experimental carcinogenesis and Todd's name against thiamine synthesis; action mechanism of central nervous system depressors ignores McIlwain's most vital contributions, and the difference between curare and curareform drugs and the methonium compounds is not sufficiently brought out; it is also a pity that little is said about the cannabinols mentioned only under "Analeptics", and very briefly under "Drugs for Hyperkinetic Disorders", although the synthetic derivatives represent an interesting and early group of psychopharmacological agents (formula 23-X and the name 'cannabadiol' are incorrect). Finally, an alphabetical list of authors after the subject index would have helped enormously if looking for specific references.

As said in my review of the first edition (*Research*, 4, 438; 1951) it is easy to criticize, but a very difficult task to write, such a book, and I should add even more so to edit the new version with its many improvements and attractive features.

F. BERGEL

BIRDS AND MEN IN BORNEO

The Birds of Borneo

By Bertram E. Smythies. With special chapters by Tom Harrisson, Lord Medway, and J. D. Freeman. Pp. xvi+562+99 plates. (Edinburgh and London: Oliver and Boyd, Ltd., 1960.) 84*s*. net.

THIS is a very unusual bird book. The main body of the work (about 460 pages) consists of a detailed systematic account of all the 549 species of birds that have been found in Borneo. It is written with the competence and thoroughness that distinguishes the author's previous volume on the birds of Burma. The articles dealing with the regular members of the fauna give the world distribution and Bornean status of each species, an adequate description, and discuss the habits, voice, food, and nest and eggs; the irregular visitors and casuals are treated more briefly. Appendixes contain the history of Bornean ornithology, an exhaustive bibliography, indexes of place-names, and of Malay and Iban names; and there is a large folding topographical sketch-map of Borneo. The illustrations, which are of very high quality, consist of 29 photographic plates and 50 plates in colour depicting 434 species from drawings by Commander A. M. Hughes.

But it is the hundred pages that precede this excellent treatise that put this book in a class apart. The first three chapters comprise an introduction, a topographical description of Borneo, with a discussion of the varied habitats that the island provides, and an account of bird migration in Borneo. These are followed by four chapters of ornitho-anthropology by Mr. Tom Harrisson, Lord Medway, and Dr. J. D. Freeman which are of the greatest interest. Harrisson says: "There is probably no other part of the world where birds and men are more intimately mixed than in Borneo", and goes on to discuss "Man v. Bird v. Man", "Man-Bird double-thinking" and many other matters, from Borneo's wild men and their bird values to hornbill ivory (more precious than jade), feather jewellery, and birds and the human stomach. This chapter overflows with information and ideas, and though it would gain in clarity with fewer parentheses it would lose much of its characteristic style. Lord Medway's chapter gives a fascinating account of the cave swiftlets, the saliva-built nests of which are the edible birds' nests of commerce, and which echo-navigate in the

darkness of the caves where millions congregate to breed. Harrisson remarks that Governments "by some complicated zoo-geology, claim the guano as a mineral and allow extraction (for fertilizer) under licence. Thus what comes out of the swiftlets' mouth as spit is succinctly dissociated from what comes out of the other end". The chapters by Dr. Freeman cover Iban augury, "the interpretation of divine revelation as it is believed to be manifested in the behaviour of certain sacred birds", and the hornbill ritual of the Iban of Sarawak. The first part of the book is illustrated with 19 plates, two of them in colour.

The publishers are to be congratulated on the excellent standard of production, worthy of this valuable addition to ornithological literature.

L. Harrison Matthews

VEGETATION AND FOREST TREES OF GHANA

Synecology and Silviculture in Ghana

By Dr. Charles J. Taylor. Pp. xi+418+120 plates. (Edinburgh and London: Thomas Nelson and Sons, Ltd., 1960. Published on behalf of The University College of Ghana.) 100s. net.

THE title of this book is unfortunate, despite its euphony, because to many potential readers it will suggest something penetrating far deeper into ecological phenomena and sylvicultural practice than was ever intended, and so leave them unjustifiably disappointed. The book consists chiefly of descriptions and notes on about 160 economically or ecologically important tree-species of the Ghana rain forest. About half the letterpress devoted to each species describes its visible features; the remainder, its habitat, distribution, phenology, and, where appropriate, its sylvicultural behaviour or treatment, and its seed and seedling. The descriptions are aided by numerous photographs and drawings which doubtless account for the high cost of the book. The line drawings are less finished than many which have been published, but most of them are adequate. It is a pity that some of the drawings of seedlings are the least satisfactory (for example, *Guarea cedrata*, *Pterygota macrocarpa*), for it is sometimes impossible to tell from them what shape the cotyledons are, and in particular whether they are thin or fleshy. The photographs form a very useful collection, and represent an amount of work which only those with experience of photography in rain forest will appreciate.

This systematic part, which forms about three-quarters of the whole, is prefaced by a brief outline of the history, topography, soils, climate and vegetation of Ghana, excellent in its way, but somewhat disjointed and with little relevance to what follows. This general matter will be useful—but doubtfully worth £5—to students of geography or botany. Dr. Taylor writes with generally commendable simplicity, though occasionally his language becomes a little too simple for accuracy, and some ecological terms (for example, plagiosere), are used incorrectly.

The style and content of the book show that it is intended for use chiefly in Ghana. Here the book will undoubtedly be an invaluable companion to ecologists and foresters; elsewhere in the West African rain forest it will be useful chiefly for its descriptions of 'slash' and other field characters, and of seedlings. Although it is not a flora, one of its principal uses will undoubtedly be for naming trees, for which it could be greatly improved by (*a*) referring in the text to the plates, (*b*) by stressing (for example, by italics) the most useful diagnostic characters, and (*c*) by adding some kind of key or summary-table which would help the beginner in knowing which family to consult.

The book is well produced and contains very few misprints.

E. W. Jones

THE CONVOLUTION TRANSFORM

Operational Calculus

By Prof. Jan Mikusiński. (International Series of Monographs on Pure and Applied Mathematics, Vol. 8.) Pp. 495. (London and New York: Pergamon Press; Warszawa: Panstwowe Wydawnictwo Naukowe, 1959.) 100s. net.

THERE are many ways of developing the transform calculus, all more or less formally equivalent. Mikusiński's starting point is somewhat uncommon: the convolution of two functions $a(t), b(t)$ is

$$\int_0^t a(t-u)\,b(u)\,du$$

which he writes as ab. Since

$$ab + ac = a(b+c),\quad ab = ba,\quad (ab)c = a(bc)$$

while ab is not identically zero unless $a(t)$ or $b(t)$ is identically zero (Titchmarsh's theorem), we have an algebraic structure which is similar to Volterra's algebra of composition, and a formulation which is equivalent to Heaviside's 'algebrization' of functional operations. There are some differences, for convolutions exist over the class of continuous functions, whereas the existence of the Laplace transform requires an order condition. There is also an early difficulty, for if a and b are constants, does ab mean their arithmetic product or their convolution abt? Volterra used a special notation $a*b*$, while Mikusiński gets over the ambiguity by distinguishing the functional form $\{f(t)\}$ from the functional value $f(t)$; once one gets used to this, the calculus is simple and effective, though the reader will find it necessary at a later page to pay special attention to the introduction of operational functions.

There are plenty of applications, to electric circuits, statics of beams, vibrations, the heat and cable equations, and a good supply of exercises. Those who know the earlier Polish, Russian or German versions will appreciate the appendix of a hundred pages in the English edition, for this not only carries certain applications further, and provides on the theoretical side a link with Banach spaces, but, even more usefully, adds details to complete certain proofs which are only sketched in the main text. While perhaps the young student should stick to one line of approach to the operational calculus, his teacher should select such a line for him from a knowledge of alternatives; Mikusiński's book provides a very pleasant account, worth studying for its own sake and for comparison with more familiar formulations of this calculus.

T. A. A. Broadbent

BETTER OPPORTUNITIES IN TECHNICAL EDUCATION

By Dr. P. F. R. VENABLES

Principal, College of Advanced Technology, Birmingham

THE second White Paper, with this encouraging title, was published in January*, nearly five years after the first White Paper on Technical Education. Much has happened in this intervening period, both in implementing the first and in determining the character of the second White Paper, and they must perforce be considered together.

The policy of the first White Paper was to establish a new four-tier structure in technical education, of local and area colleges, then regional colleges and, at the apex, the colleges of advanced technology, which were to be the main means of producing the much-needed technologists. The second White Paper directly affects the work and development of the first three levels of colleges because it contains proposals for a major reconstruction of the system of courses for technicians, craftsmen and operatives provided by them. Of the factors which have prompted these proposals, three have been dominant: The first is the need to supply more technical education for the greatly increased number of young people soon coming into employment; secondly, the need to smooth the transition from school to college; and thirdly, the need to reduce greatly the wastage in part-time courses made evident by the Crowther Report. The question is whether the proposals, and the means to implement them, are commensurate with the needs of the times.

The main proposals are summarized as follows:

(1) Students should start at a technical college immediately after leaving school. Preliminary courses in evening institutes should be discontinued.

(2) More care should be taken in the selection of students for courses. Colleges should experiment with full-time induction courses and with tutorials.

(3) The courses will include: (*a*) National Certificate and Diploma courses for students aiming to become at least high-grade technicians; (*b*) Technician courses devised specifically for particular industries; (*c*) Craft courses; (*d*) Courses for operatives.

(4) Ordinary National Certificate courses will last two, instead of three, years. The standards of entry will be raised either by insisting on four General Certificate of Education (Ordinary Level) subjects, or by passing the sessional examinations of the new general courses which will be introduced. These general courses may lead also to technician courses.

(5) Craft courses will be modified in various ways, for example, by broadening their content, and in replacing City and Guilds Intermediate by Craft Certificates; and courses for operatives should be vigorously developed.

(6) More time should be provided under day-release schemes by extending the session to the county college year of 330 hr. per annum, as specified in the 1944 Education Act, and the gain in time should be spent on general education. No student should have to rely wholly on evening study.

(7) Sandwich courses (especially for technicians) and block-release courses should be increasingly developed.

The proposals include no novelties—day-release courses are at least forty years old, sandwich courses nearly sixty years old, the county college idea more than forty years old, though the much fewer courses for operatives and block-release courses are more recent in origin. The White Paper, therefore, is to be regarded as extending the application of well-established ideas and increasing the support given to them, especially from industry. In its summary, the White Paper gives too optimistic an impression in stating that "About half a million students are attending the courses at present, and the Government look forward to a big increase in their number". A realistic basis for judging the present position and future tasks is to compare two facts: while the numbers in part-time day-release courses increased tenfold from 1938–39 to 1958–59, the numbers of students of 'County College age' still only reach about 17 per cent of the total age group (15, 16, 17 years) in employment. In short, after a ten-fold expansion over so long a time, we still have about six times as far to go 'on a voluntary basis' to include all who should be in county colleges: and by no means all the 17 per cent will be affected by this White Paper.

Significant though they are in mitigating the rigours of the part-time route, the proposals should, therefore, not be allowed to obscure the far greater advantages that would accrue to the whole age group were the recommendations of the Crowther Report implemented of both raising the school-leaving age and establishing county colleges. The White Paper admits that: "In a system of voluntary part-time courses there are limits to what can be done". With more candour, it would have inserted the word 'severe' before 'limits', for the awkward unpalatable problems remain, namely, those described by the Crowther Report as "The Need for Time" and "The Need for Breadth". The severe limits apply both to the content of the courses and to the support they are likely to attract from industry, especially among the 73·5 per cent of 56,000 manufacturing firms each of which has less than a hundred employees.

The White Paper can, of course, only suggest a general pattern within which the many bodies responsible for the actual planning and provision of courses must do their work. Many hundreds of existing courses will need to be modified, and many new ones developed, especially for technicians and operatives. This essential task is being tackled with a commendable sense of urgency by the City and

* Better Opportunities in Technical Education. Pp. 24. (Cmnd. 1254.) (London: H.M.S.O, 1961.) 1*s.* 3*d.* net.

Guilds of London Institute, the Regional Examining Unions, the Joint Committees and so on, and there is little doubt that these long-standing partnerships in technical education will achieve what is possible within the limited time-tables set by the proposals.

It is difficult to be sanguine as to whether the other means required are commensurate with the needs of the next decade. The first White Paper gladdened the hearts of those engaged in technical education by definitely allocating £97 million for the expansion it envisaged, and another £45 million were added in 1959, whereas no estimate of additional cost is given in the second White Paper. It might well be argued that the original target of doubling the then day-release figure of 330,000 by the mid 1960's is allowed for, or nearly so, in the building programme covered by the foregoing sums. Perhaps it is for this reason that the White Paper expresses the opinion on the cost that "relatively to the total expenditure on technical education this should be small"; and this despite the fact that the number of teachers engaged in technical education is likely at least to double in the next ten years without any effects of this White Paper being taken into account. Furthermore, the White Paper envisages a big increase in half a million students, but should this merely be up to the original 660,000, especially when attendance at evening institute courses is to be discontinued and block-release and sandwich courses are to be increased. In the latter types of courses, two students will use the space (and teaching strength) of five part-time day students with consequent increase in expenditure. The effect will be even greater in providing workshops in block-release and sandwich courses with a high proportion of practical work. In view of the sentence about expenditure quoted above, a sceptic, knowing the rearguard actions fought in the history of technical education, might justifiably conclude that the effect of the White Paper will prove to be no more than a desirable reduction of the rigours of an outmoded part-time route, supplemented by some sandwich courses, rather than the rapid replacement of it up to 18 years of age by technical education in full-time and sandwich courses. If the latter were strongly pressed forward with really adequate means instead of just bringing the past up to date, then a notable advance to meet the rising demands of the next decade would be achieved.

GOLDEN JUBILEE OF THE BIOCHEMICAL SOCIETY

By Dr. P. N. CAMPBELL and Dr. W. J. WHELAN

Honorary Secretaries

THE first meeting of the Biochemical Club was held at University College, London, on March 4, 1911. After the Club had acquired *The Biochemical Journal* in 1913 it changed its name to the Biochemical Society. This week, therefore, sees the fiftieth anniversary of the foundation of a Society instituted solely for the advancement of the science of biochemistry. We are glad to have the opportunity to survey, briefly, the past history of the Society and to look to the future.

Early Days

On reading the *History* of the Society, prepared by R. H. A. Plimmer in 1949, one is conscious of the fact that, although the Society has grown enormously, its character has altered very little. It was from the start decided that the practice of the Physiological Society should be adopted and that the Society should meet at various laboratories. During the first year, eight meetings were held, and by the time of the first annual general meeting there were 132 members. The next year was taken up with the negotiations for the purchase of the *Journal* from Benjamin Moore, the first professor of biochemistry in Great Britain, who had founded it in 1906. A poll of the members in 1912 resulted in the decision to make membership involve compulsory subscription to the *Journal*, and so the subscription was raised from 10*s*. 6*d*. to 25*s*. per annum. The Cambridge University Press has been responsible for printing and publishing the *Journal* since 1913.

In the first few years the Society made a small profit, but after the First World War the cost of publication rose and grants were received from the Royal Society and other sources. At this stage the subscription was raised, first to 35*s*. and then to 42*s*. It was many years later, in 1953, that the last change was made to 70*s*. The present sound financial state of the Society, which does not depend on any form of subsidy, is due in the first place to J. A. Gardner, who served as honorary treasurer during 1913–43.

Personalities within the Society

The early years of the Society were marked by long periods of devoted service on the part of its officers. Such extended service would not be possible to-day because of the size of the Society, which now finds it necessary to rent offices and to employ a professional staff to organize its affairs. These are only very recent developments, and for the first forty years of its existence the only premises the Society could be said to have were the offices and laboratories of its honorary officers. J. A. Gardner's long service as treasurer was matched by A. Harden's editorship of the Society's *Journal* during 1913–37.

The first chairman of the Society's committee was F. Gowland Hopkins, and his services to biochemistry were commemorated by the Society in 1958 by the endowment of the Sir Frederick Gowland Hopkins Memorial Lecture. The third of these lectures will be given by Sir Hans Krebs at the Royal Institution on March 28. The Society also shows its gratitude for outstanding service by the

election of honorary members, and those so elected have been W. D. Halliburton (1923), A. Harden (1938), Sir Frederick Gowland Hopkins and R. H. A. Plimmer (1943), Sir Charles Martin (1951), Sir Henry Dale (1958) and Sir Rudolph Peters (1959).

Membership

Membership of the Society is open to all those who are interested in biochemistry, and is not confined to those who reside in the United Kingdom. In fact, more than 30 per cent of the present members live overseas. The total membership passed the 1,000 mark in 1944, and at the present figure of 3,000 has doubled in the past ten years. This means that the Society is the largest of its kind in the world.

Role in International Biochemistry

Since the Society's membership is world-wide, it is natural that it should be interested in international relations among biochemists. In 1948, the Society sent out an inquiry concerning the desirability of holding an international congress of biochemistry. The response was so favourable that the Society took the initiative and organized the first International Congress of Biochemistry, held in Cambridge in August 1949. At this time there was no international union of biochemistry, and the first Congress had the backing of the International Union of Chemistry. In this year (1961), when we look forward to attending the fifth of these congresses, to be held in Moscow in August, it is with pleasure that we recall the initiative of those who worked hard for the first congress.

After the success of the first congress, strenuous efforts were made to found an International Union of Biochemistry recognized by the International Council of Scientific Unions. These efforts were eventually successful in August 1955.

Although these large international congresses have much merit, there is also a case for holding smaller meetings on a more limited scale. The joint meetings which the Society holds with its sister societies in Europe come into this category. It has now become the custom to hold one of these meetings during the years when there is no international congress. Through these meetings, biochemists in Great Britain are able to make personal contacts with those in Europe. For our part, we offer a special invitation to European biochemists to attend the summer meeting of the Society which is held each year, either in Oxford or in Cambridge.

Meetings

The policy of holding meetings for the presentation of original contributions has changed very little since the early days of the Society. A member has the right, and is indeed encouraged, to present the results of his work before a meeting of other members of the Society. This is an important aspect of the work of the Society, and last year 260 papers were presented in this way. It is also useful, however, occasionally to discuss some particular aspect of the subject at greater length, and it was with this in mind that a series of symposia were initiated in 1947, the proceedings of which are published. So far twenty of these symposia have been held.

In addition to the two types of meeting already described, colloquia are held at which work on a particular research project is discussed. This type of meeting is normally held in conjunction with an ordinary meeting of the Society, and serves to direct attention to the work of the department being visited. The number of scientific meetings of all types reaches 404 at the fiftieth anniversary meeting.

Publications

One of the most important activities of the Society is the publication of *The Biochemical Journal*, in which are to be found many papers now regarded as classical landmarks in the development of the subject. Prof. Moore founded his *Journal* in 1906, because of his desire that contributions should be published as submitted without criticism or editorial suggestions. Much of his reluctance in parting with the *Journal* to the Society was due to his fear that this policy would be changed by the Society, and it cannot be denied that his fears were well founded. In fact, ever since the acquisition of the *Journal* in 1913 the editorial policy has been strict. This policy has helped to establish a tradition of care and proficiency in biochemical laboratories.

Within the high standard set for the acceptance of papers for the *Journal*, the policy of the Society is for the *Journal* to publish all papers submitted for publication which come within the subject of biochemistry. Authors do not have to be members of the Society. With the expansion of the subject this policy has led to an enlargement of the *Journal*, so that while in 1950 1,279 pages were published, the corresponding figures for 1955 and 1960 were 2,112 and 2,510 pages respectively. The circulation has also expanded, and there are to-day more than three thousand subscribers who are not members. This means that the *Journal* probably has a larger total circulation than any other journal devoted entirely to biochemistry.

During 1957 the committee of the Society carefully considered whether the Society should expand its publishing activities. As a result of these discussions, it was decided that clinical biochemistry was not adequately covered, and the Society eventually became the joint owners with the Medical Research Society of *Clinical Science*. This journal is now published by the Cambridge University Press, and we look to its playing an increasing part in the work of clinical biochemists in Great Britain and overseas.

The Future

In considering the future it seems likely that the activities of the Society will expand most in directions which are concerned with the status of the subject in the universities. If biochemical research is to flourish in Britain, not only shall we need to attract the best students to the departments which now have a first-degree course in biochemistry, but also more departments must be created, both for teaching and research. Last year a booklet was published on *Careers in Biochemistry*, its aim being to provide full information on training, opportunities and prospects, for the benefit of potential students and their advisers. A series of discussions is being held on various aspects of the subject. For example, at a joint meeting with the British Association, in

September 1960, a symposium was held on "The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain". The proceedings of this discussion have now been published by the Society. Later this year, at Oxford, it is planned to discuss the problems of teaching biochemistry to undergraduates.

Mention has already been made of the recent changes in the administration of the Society's affairs, largely a consequence of the rapid growth of its membership and of the *Journal* in the past ten years. The Society's healthy financial state has enabled these changes to take place smoothly, even to the renting of premises at the very high charges prevailing in central London. Not all the necessary changes can, however, be made so easily. The size of the audiences at the Society's symposia, held in London, makes it impossible any longer to hold these in many institutions which for long have acted as hosts. It is obvious that biochemistry is in a period of rapid expansion the limit of which is not yet set, and problems of accommodation will become increasingly acute. This is part of a wider problem, and the need to take action was realized after the War, with a proposal by the Government to establish a Science Centre from which learned societies could organize their affairs, centralize information, and conduct meetings. Unhappily the proposal never bore fruit; but its fulfilment would be one of the boldest moves in advancing science in Great Britain.

The main hope for the future must be that, in spite of the expanding activities of the Society, it will be able to remain reasonably informal so that there can be a ready exchange of ideas, both scientific and administrative. By this means it is hoped that the Biochemical Society will continue to play its part in the development of a still comparatively new and exciting science.

GENE EVOLUTION AND THE HÆMOGLOBINS

By Prof. VERNON M. INGRAM

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THE four types of polypeptide chain which go to make up the molecules of the three normal human hæmoglobins are believed to be controlled by four independent genes[1]. The following article is an attempt to discuss the chemical and genetic relationship between these chains from an evolutionary point of view; to a lesser extent, because much less is known, the hæmoglobins of other vertebrates will also be mentioned. It should be emphasized that the main purpose of this discussion, and of the evolutionary scheme to be proposed, is to provide a basis for the discussion of the evolution of genes in general and hæmoglobin genes in particular. Questions are raised which will, in part, be answered soon by the chemical work on vertebrate hæmoglobins which is now proceeding in various laboratories (see, for example, ref. 2).

The study of the chemistry of the human hæmoglobins has already provided evidence of the kind of phenotypic effects to be expected from gene mutations as, for example, in the known single amino-acid substitutions in the peptide chains of abnormal hæmoglobins[1]. It is on such changes in protein structure that the forces of natural selection are assumed to act. From the evolutionary and the practical point of view it is convenient to study a commonly occurring protein, such as hæmoglobin, which is found in all vertebrates. Hæmoglobin is not only accessible for chemical study but is also sure to have played an important part in vertebrate evolution, because of its vital physiological function as the carrier of oxygen.

Most of the discussion which follows will centre around the chemical findings in the human hæmoglobins, since they are by far the best studied of vertebrate hæmoglobins. However, the basic similarities in chemical structure between man's hæmoglobins and those of other mammals and lower vertebrates are very striking[3]. All known vertebrate hæmoglobins—except those of the lamprey and the hagfish—are built on the same molecular pattern: they consist of four polypeptide chains of roughly 17,000 molecular weight, with one hæm group each. The hæmoglobin of the lamprey is peculiar in consisting of a single polypeptide chain of molecular weight 17,000. The hagfish hæmoglobin appears to be similar, or possibly a dimer of 34,000 molecular weight[3].

The peptide chains in the other vertebrates are of two different types; for example, human adult hæmoglobin consists of two so-called α-chains and two β-chains. There is usually interaction between the four hæm groups in their reaction with molecular oxygen; in other words, a plot of the degree of oxygenation of the hæmoglobin molecules against the partial pressure of oxygen is sigmoid in shape[4]. This fact enhances enormously the physiological efficiency of the hæmoglobin molecule as our oxygen carrier[5], since it favours complete saturation with oxygen in the lungs and complete discharge in the tissues. This great similarity which characterizes most vertebrate hæmoglobins suggests that we are studying that aspect of the evolution of a particular protein molecule which is concerned with detailed development of an already well-defined molecule. It is true that the hæmoglobin quadruples its size during this evolution (if we include the lamprey hæmoglobin), but the change is due to the aggregation of four fairly similar protein sub-units (peptide chains), rather than to an actual lengthening of a molecule. In the evolutionary scheme to be discussed it is suggested that the increase in complexity, and in diversity, of the hæmoglobins is an illustration of a more general process of gene evolution which results in an increase of the number of genes.

Human Hæmoglobins

The following striking situation is found in the human hæmoglobins:

(1) The three normal human hæmoglobins all possess a common half-molecule which may be written $-\alpha_2A$. This formulation indicates that this half-molecule unit is composed of two normal α-peptide chains as first described for normal adult hæmoglobin A. However, the other half of each of the three hæmoglobins consists of different types of peptide chain, β, γ or δ, one type for each hæmoglobin. All four chains are of roughly equal size with a chain molecular weight of about 17,000. These three hæmoglobins may be formulated as follows:

Adult	= hæmoglobin A	$= \alpha_2A\beta_2A$
Fœtal	= hæmoglobin F	$= \alpha_2A\gamma_2F$
Kunkel's minor component[4]	= hæmoglobin A_2	$= \alpha_2A\delta_2A$[5]

This list may have to be extended as the study of other minor hæmoglobins continues[7].

I postulate[1] that four genes are involved in the manufacture of these peptide chains, so that the *genotype* of a normal individual may be written as:

$$\alpha A/\alpha A,\ \beta A/\beta A,\ \gamma F/\gamma F,\ \delta A_2/\delta A_2.$$

In this view the products of the α-genes are common to all the human hæmoglobins.

(2) In total amino-acid composition[8] the four types of chains compare as follows:

αA and βA	= differ in perhaps 21 out of nearly 140 amino-acids
γF and βA	= differ in perhaps 23 out of nearly 140 amino-acids
δA_2 and βA	= differ in less than 10 amino-acids.

In addition, γF is the only one of these chains to contain the amino-acid *iso*leucine—four residues per chain.

(3) The αA-chain begins with the amino-acid sequence[7] Val-Leu- . . . ; the βA-chain and the δA_2-chain begin with Val-His-Leu . . . . The γF-chain begins with the sequence Gly-His-Phe-, which although different from the β-chain shows a clear affinity in the type of amino-acid with the beginning of the βA-chain. In both cases, the first amino-acid is neutral and aliphatic, the second is the basic amino-acid histidine, and the third has a non-polar side-chain.

The peptide chain beginning with the Val-Leu- sequence (α-chain) has a counterpart[3] not only in all known mammalian hæmoglobins but also in the hæmoglobins of all the lower vertebrates so far examined, except for the hæmoglobin of the lamprey. This is not to say that the Val-Leu- chains of other animals resemble the human chain precisely, but rather that there might be a strong 'family resemblance'. It is of interest to attempt to explain the repeated occurrence and strange similarity of the Val-Leu- (the α) chain in the vertebrates.

The following postulates are used in developing a scheme for the evolution of the hæmoglobin genes.

Postulate 1. Mutations of a gene result in either single or multiple amino-acid substitutions in the peptide chain which that gene controls, or inversions of part of the amino-acid sequence, or a combination of these possibilities. The new hæmoglobin peptide chains produced by such mutations are then either favoured or discarded in the course of natural selection.

Postulate 2. At several points in the course of evolution a gene for a particular hæmoglobin peptide chain has undergone *duplication*, followed by, or simultaneous with, translocation. The two initially equivalent genes have then evolved independently, governed by the selective pressure of their environment on their protein products. Such mechanisms have been previously postulated: for example, ref. 9. The role of gene duplication[9,10] in evolution has been discussed by Stephens[11]. His conclusion was that the case for duplication as an important factor in evolution was so far neither proved nor disproved.

It is of course equally possible to postulate the occurrence of chromosome duplication, with subsequent independent evolution of the initially identical chromosomes. Such a scheme would fit into the proposed hypothesis equally well.

It seems likely that α-, β- and γ-genes are located on different chromosomes, since they segregate independently, whereas β- and δ-genes appear to be linked[12].

Postulate 3. Once the α-chain, or rather the α_2-dimer, is required to fit precisely with at least two other dimers—β_2 and γ_2—the α-chain is no longer as free to be varied by mutation. It has become 'conservative' and its rate of evolution will be less than that of the other chains, as is perhaps seen in the persistence of the Val-Leu- beginning of the α-chain of the vertebrates.

In addition, one can postulate that mutations of the α-gene produce mutant α-chains which are more severely selected against in the later stages of evolution than are mutants of other chains. This is likely to be so, because in the later stages of evolution the α-chains participate in the formation of fœtal hæmoglobin, a vulnerable point in the life-cycle of the animal. It is a fact that mutants of the human α-chain never reach a high frequency of distribution, in contrast to some β-chain mutants, although we know of as many different kinds of α-chain mutants as of β-chain mutants.

Scheme for the Evolution of the Hæmoglobin Genes

We might suppose that originally the hæmoglobin molecule was rather like the present-day myoglobin molecule, that is, that it had a single peptide chain with a single hæm group, and that therefore it could not show hæm-hæm interaction. The size of this molecule might vary, but eventually it might be stabilized at a value of around 17,000 molecular weight.

At this stage of evolution, presumably earlier than the teleost fishes, the hæm protein inside the muscle cells is assumed to be the same as that in the circulation. The muscle hæm protein became myoglobin in the course of evolution; it retained a molecular weight of 17,000 and a complexity of only one hæm group and one peptide chain per molecule. It was, of course, still subject to mutational changes, as can be seen from the fact that its present-day amino-acid composition and sequence in a given animal often differs considerably from that of any of the analogous hæmoglobin chains[13]. For example, human myoglobin contains *iso*leucine, but no cysteine, whereas the reverse is true of human adult hæmoglobin.

On the other hand, one can foresee limits to the kind of mutations which would be tolerated. The X-ray studies of Kendrew[14] and of Perutz[15] show that the three-dimensional arrangement of chains in myoglobin and the hæmoglobin sub-units (also of

17,000 molecular weight) are remarkably similar, though not identical. This statement applies also to the two kinds of sub-units found in haemoglobin itself. Presumably, mutational alterations in the course of evolution which would drastically affect the three-dimensional structure were not tolerated. Such considerations imply that the configuration of the peptide chains in myoglobin and haemoglobin became stabilized early in evolutionary history, at least in its most important features.

During the evolution of the primitive haemoglobin chain—provisionally called the 'α'-chain—there occurred a gene duplication followed or accompanied by translocation. From now on the two duplicate 'α'-chain genes could evolve independently—one to become the modern myoglobin gene, the other to become the α-chain gene of present-day haemoglobin. Eventually, according to the scheme, the α-chain gene would evolve in such a way that its product, the α-chain, had the property of dimerization in solution to form α_2 molecules. Such a property would be favoured strongly, if it entailed, in addition, the possibility of haem–haem interaction between the two haem groups of the new dimer molecule and therefore the possibility of more efficient oxygenation and deoxygenation. Once produced, such a mutation is unlikely to be lost in the further evolution of haemoglobin.

At this stage, the sequence of the 'α'-chains is still variable within the dictates of structural requirements, since there is nothing yet to put additional restrictions on it.

We might next postulate that the genes of the α_2-chains duplicated again. After this gene duplication two types of dimer—α_2 and γ_2—would evolve side by side. Sooner or later, these chains would have evolved sufficiently to be able to form tetramers with even greater selective advantage because of the increased haem–haem interaction likely to be found in such tetramers. The characteristics of the genes responsible for the ability of the chains to form tetramers would certainly be fixed. This stage of haemoglobin evolution seems to have been reached already in some teleost fishes, because they already possess a four-chain haemoglobin[3].

The third gene duplication and translocation is pictured as occurring with the γ-chain gene, giving rise to a new γ-gene destined to evolve into the β-chain gene. At this gene duplication the property of forming tetramers is already firmly established. The new gene can develop along its own line to provide a haemoglobin tetramer—$\alpha_2\beta_2$—particularly adapted for the adult body. On the other hand, the old γ-chain continues to develop and to provide half the molecule of the fœtal haemoglobin ($\alpha_2\gamma_2$). It is the γ-chain gene, rather than the α-chain gene, which is said to duplicate here, because the γ-chain dimers, γ_2, have already the necessary complementariness for forming tetramers with α_2. This complementariness will be automatically a property of the product of the new gene. In addition, we shall see later that β- and γ-chains are more closely related to one another than either is to the α-chain. Therefore we might consider them to have diverged at a later stage.

At this point of evolution, three independent genes—α, β, γ—are assumed to be present, each one capable of forming chains which dimerize and which aggregate to the tetramers $\alpha_2\beta_2$ or $\alpha_2\gamma_2$. Haem–haem interaction is strongly present in the tetramers. Such a situation has an important effect on the further

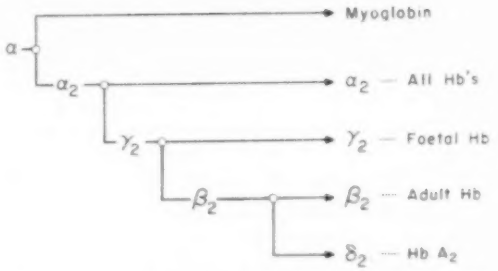

Fig. 1. Evolution of the haemoglobin chains. The α-chain is the ancestral peptide chain. —○— indicates a point of gene duplication followed by translocation of the new gene

evolution of the α-chain. This chain, or rather its dimer, α_2, is required to fit with two different partners, β_2 and γ_2. As a result, less variation is allowed to the α-chain; it has become 'conservative'. Perhaps such conservation is in part responsible for the apparently universal presence of α-chains beginning with Val-Leu- in the haemoglobins of the higher vertebrates. There is an alternative explanation for the apparently greater stability of the α-genes: this gene controls also the fœtal haemoglobin and therefore may not undergo extensive mutational alterations, since the fœtus is a much more delicate organism. The very fact that any alteration in the α-chain gene, and therefore in the α-chain, seems to affect all types of haemoglobin may be sufficient to explain the apparent 'conservatism'.

On the other hand, there is no *a priori* reason why different parts of a molecule as complex as a protein should develop at the same rate. The difference in apparent stability between the α-chain and the others could be no more than what would be expected as normal variation. It will be interesting to see just how similar the Val-Leu- chains of different vertebrates are.

At the fourth and last gene-duplication in the scheme we suppose that it is the β-gene which becomes duplicate, leading to the δ-chain genes controlling the δ-chains of haemoglobin A_2. The origin of this δ-chain is placed near the end of the evolutionary scheme, because of its great chemical similarity to the β-chain[16]. Furthermore, the presence of a haemoglobin A_2-like component seems to be confined to the higher primates[17]. In this view, haemoglobin A_2 is a new haemoglobin rather than an archaic one, as has often been supposed. It has been reported to have a higher affinity for oxygen[18] and perhaps it is a more efficient haemoglobin, destined to replace eventually $\alpha_2\beta_2$ (ref. 19). Its proportion is certainly doubled in some thalassæmias[17], perhaps as a compensating mechanism. There is genetic evidence that the genes for δ- and for β-chains are linked[12], indicating perhaps that the process of translocation of the new δ-gene has not yet occurred.

Where does the lamprey fit into this scheme? One form, *Petromyzon planeri*, has two fœtal and two (different) adult haemoglobins[20]. The molecular weight of the adult mixture is given as 17,000 (ref. 3). Perhaps these lamprey haemoglobins are the result of an independent evolution scheme similar to the one discussed in the present article, but which has never included the mutations which led to the formation of dimers and tetramers. We might regard the lampreys as having branched off before or just after

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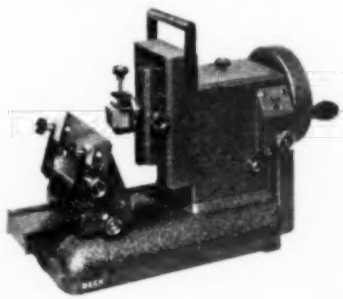

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Table 1. Comparison of the N-terminal Sequences of the α- and β-Peptide Chains of Human Haemoglobin A.[21]

α-chain	Val-	Leu-	Ser-	Pro-	Ala-	Asp-	**Lys**-	Thr-	Asp-	Val-	**Lys**-	Ala-	Ala-	Trp-	Gly-	**Lys**-	Val-	Gly-	Ala-	His-	Ala-	Gly-	Glu-	Tyr-	Gly-	(Ala,Glu)-	Ala-	Leu-	Glu-	**Arg**-
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
	Met-	Phe-	Leu-	Ser-	Phe-	Thr-	Pro-	Thr-	**Lys**-																					
	32	33	34	35	36	37	38	39	40																					
β-chain	Val-	His-	Leu-	Thr-	Pro-	Glu-	Glu-	**Lys**-	Ser-	Ala-	Val-	Thr-	Ala-	Leu-	Trp-	Gly-	**Lys**-	Val-	Asp-	Val-	Asp-	Glu-	Val-	Gly-	Gly-	Glu-	Ala-	Leu-	Gly-	**Arg**-	Leu-
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

the first gene duplication in the scheme of Fig. 1. Unfortunately, nothing seems to be known about the presence or absence of a separate myoglobin in the lampreys.

Discussion

The proposed scheme expresses a desire to explain the striking chemical similarity between α, β, γ and δ human haemoglobin chains in terms of their evolution from a common precursor.

Braunitzer *et al.*[21] have published some preliminary findings of the amino-acid sequences in the first 30–40 positions of the human α- and β-chains (Table 1). Between the two sequences there is a strong 'family resemblance' of the degree expected for two gene products which have evolved independently, but from a common ancestor. Also Gratzer and Allison[3] have very recently discussed the possibility that the haemoglobin chains might have evolved from a common ancestor.

It has been suggested to me that the four genes controlling the four chains might have evolved from four unrelated genes which originally controlled the synthesis of quite unrelated proteins; thus there would have been no increase in the total number of genes. By a process of parallel evolution—successive and independent mutations—each of these four genes eventually changed so that it made one of the haemoglobin peptide chains. The last stages of evolution, when pairs of genes were involved in producing parts of a complex molecule, must then be called on to produce similarity in chemical structure and in configuration. It is easy to conceive of a selective mechanism which would favour changes in various members of a molecular aggregate, such that the members might fit together better. However, it is hard to think of such a mechanism also selecting for chemical and structural similarity of the monomers. In addition, the ability to dimerize would have to arise *de novo* four times, an unlikely situation.

Although we cannot at the moment completely reject the idea of parallel evolution of the four genes from unrelated genes, it is not a very palatable one. The similarity between the human α-, β-, γ- and δ-chains is so great: the C-terminus of the chains ends with the sequence -tyrosyl-histidine or -tyrosyl-arginine[10,22]; their common ability to incorporate an active haem group; their similar folding and chain length[14,15]; absence of *iso*leucine in α, β and δ[8,16]; and so forth. Altogether, an evolution from a common ancestor is more attractive.

Chemical Evolutionary Relationship Between the Chains

How many mutational steps occurred between the original 'α'-gene and the present-day human α-gene? Or between the original 'α'-gene and the human β-gene? It is more meaningful, perhaps, to ask how many mutational events might separate the present-day human α- and β-genes. Out of 140 amino-acids, we know from the composition that approximately 20 are different. This gives a minimum of 20 mutations of the kind effecting single amino-acid substitutions.

It is believed that the evolution of the vertebrates began some 5×10^8 years ago. Let us assume a mean generation life of 5 years among the vertebrates, which implies some 10^8 generations for the evolution of vertebrate haemoglobins. A generally acceptable rate[23] per generation is 10^{-8}–10^{-9}, which leads to a figure of 100–1,000 mutations in the evolutionary history of a vertebrate haemoglobin. This figure, which is itself a minimum one, is very considerably higher than the (minimum) number of mutations which appear to distinguish α-chains from β-chains and α-chains from γ-chains.

The only conclusion which can be drawn from such a calculation is that a more than sufficient number of mutational events have passed in the history of the vertebrates to account for present-day differences between the various parts of the haemoglobin molecule in the human species.

Comparison of the Fingerprints of the Human α-, β-, γ- and δ-Chains

Rather than deduce the chemical relationship between the chains from their amino-acid composition, it is better to compare their 'fingerprints'[24]. The two-dimensional maps, or fingerprints, of the tryptic peptides derived from each of these four peptide chains give at least a crude idea of the similarity and dissimilarity in their amino-acid sequences and hence of the closeness of the chemical relationship between them.

Human α-Chains and β- or γ-Chains

With the exception of peptide number 21 (ref. 25), all the peptides (some 14 for each chain) occupy different positions on the fingerprints[22] of α-chains compared with β- or γ-chains, or they can be distinguished by such methods as extended paper ionophoresis. They are therefore different in their amino-acid sequences. Peptide 22 is free lysine. It does not follow that the differing peptides of the α- and of the β- or γ-chains are totally altered. They could contain short amino-acid sequences in common[21]. In any event, the indications are that the amino-acid differences between the α- and the β- or γ- chains are distributed throughout their length.

The general comment might be made that there is a familial likeness between the distribution of peptides on the fingerprints of α-, β- and γ-chains. Surely this will reflect a structural relationship (Table 1). We would suppose that portions of their amino-acid sequences are common to all three, as is the tertiary structure of the two types of chain of horse haemoglobin, which correspond to the human α- and β-chains.

Human β-Chains and γ-Chains

Apart from peptides number 21 (a pentapeptide) and 22 (free lysine), the following peptides[25] occupy

very similar positions[23] and would be closely related, if not identical: peptides 12, 14, 15½, 19, 20½, 26. The number is an impressive proportion of the whole chain. If it is correct that these peptides are indeed identical in the β- and γ-chains, it would mean that perhaps 9 peptides out of some 14 are shared by the chains. Some of these peptides are quite long. Their position along the chains is not known, except that peptide 26 is the third one from the N-terminus[21]. These conclusions underline the chemical similarity between β- and γ-chains, which can also be deduced from their amino-acid compositions.

Human β-Chains and δ-Chains

The recent work of Stretton[18] has shown that the β-chains and the δ-chains are very closely similar in their fingerprints. In fact, out of a total of some 14 tryptic peptides, only 4 peptides are different: they are numbers 5, 12, 25 and 26. The similarity between other pairs of peptides from the β- and δ-chains has been ascertained much more carefully by amino-acid analysis than has so far been done with the γ-chains. Moreover, the differences between peptides 12, 25 and 26 from β- and from δ-chains have been shown to involve only 4 single amino-acid differences, for example, serine-threonine (in two places), threonine-asparagine, glutamic acid-alanine. These four single amino-acid differences, together with an unconfirmed fifth one, are so far the only ones definitely known between this pair of chains, each of which is some 140 residues long—a very close chemical similarity indeed.

Apart from the tryptic peptides of the α-, β-, γ- and δ-chains, there is in each case the trypsin resistant 'core' to be considered which amounts to rather more than a quarter of the chain. Here the differences between the chains are far from clear and cannot yet be usefully discussed, except to say that the 'cores' all appear to be similar.

Fingerprints of haemoglobins from other mammals (ref. 2, and Muller, C. J., unpublished) are recognizable as 'haemoglobin'. It will be interesting to compare the degree of similarity between the mammalian haemoglobins on one hand with, say, chicken or teleost haemoglobin.

Recently, Zuckerkandl[2] has shown that fingerprints of haemoglobin from the gorilla and chimpanzee are indistinguishable from those of human haemoglobin. A greater number of differing peptide spots are observed in the less closely related orang-utan and rhesus monkey. These extraordinarily interesting findings give added proof of the validity of using a chemical study of vertebrate haemoglobins to discover evolutionary relationships.

Conclusion

It appears that a sufficient number of generations has passed since the beginning of vertebrate evolution to allow for the known or suspected number of mutations which separate the α-, β- and γ-chains of human haemoglobin.

The similarity in the fingerprints between β- and γ-chains of human haemoglobin supports the suggestion that these chains diverged from one another at a later stage in evolution than either from the α-chain gene.

The close similarity between β- and δ-chains gives weight to the idea that the δ-chains of haemoglobin A_2 are a recent evolutionary development from the β-chains.

The suggestion is made that a single primitive myoglobin-like haem protein is the evolutionary forerunner of all four types of peptide chain in the present-day human haemoglobins, and of the corresponding peptide chains in other vertebrate haemoglobins. Such a scheme involves an increase in the number of haemoglobin genes from one to five by repeated gene duplication and translocations; the scheme may thus illustrate a general phenomenon in gene evolution.

I acknowledge the many stimulating discussions with Drs. C. Levinthal, S. E. Luria, C. Baglioni, A. O. W. Stretton, J. V. Neel and P. S. Gerald. I am also grateful to Drs. W. B. Gratzer and A. C. Allison for allowing me to read their review paper[3] before publication.

Two books have been particularly stimulating: J. B. S. Haldane, *The Biochemistry of Genetics*; and C. B. Anfinsen, *The Molecular Basis of Evolution*.

No serious attempt has been made to survey critically the literature on gene evolution or duplication. This is partly in order to present a clearer and more provocative hypothesis and partly because I do not feel qualified to evaluate the numerous contributions to that field. Recent experimental work on the animal haemoglobins has been admirably summarized in the Gratzer and Allison article[3].

This work was supported by grants from the National Science Foundation and the National Institutes of Health, U.S. Public Health Service.

Note added in proof. Further work by G. Braunitzer and his colleagues (*Z. physiol. Chem.*, in the press) shows that the similarity of the α- and β-chains continues throughout these chains.

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OBITUARY

Prof. J. T. Patterson

JOHN THOMAS PATTERSON, emeritus professor of zoology in the University of Texas, who died on December 4, 1960, at the age of eighty-two, will be remembered especially for his work on evolutionary genetics of *Drosophila*, published as a series of "Studies in the Genetics of Drosophila" by the University of Texas and culminating in a book, *Evolution in the Genus Drosophila* (1952), written in collaboration with Wilson S. Stone. Yet this great programme of work, involving the activities of numerous colleagues and graduate students, was initiated after he reached the age of sixty, in the evening of a long life devoted to biological teaching and research.

J. T. Patterson was born at Piqua, Ohio, on November 3, 1878. He received his bachelor of science degree from the College of Wooster in 1903 and his Ph.D. from the University of Chicago, where he was a student of C. O. Whitman, in 1908. He went to the University of Texas in Austin in 1908 as instructor in zoology, becoming adjunct professor in 1911, professor in 1913, 'distinguished professor' when this special rank was created in 1937, and emeritus professor on his retirement from teaching (but not from research) in 1955. He was one of the last of a great generation of Chicago Ph.D.'s in zoology that included such men as W. C. Allee, George Bartelmez, Carl Moore and Oscar Riddle.

When Patterson arrived at the University of Texas he found extremely primitive conditions in a frontier society. By his own efforts he built up the Department of Zoology, successively adding to the staff Carl Hartman, T. S. Painter and H. J. Muller. The bat-infested laboratory of the early years was replaced by the Biology Building in the 1920's and the magnificent Experimental Science Building in 1952. A total of thirty-one students received their M.A. degrees and twenty-nine their Ph.D.'s under Patterson's direction during the forty-eight years of his active teaching career in Texas. An extremely hard worker, he would arrive at the laboratory each morning about 6 a.m., spending the whole day in the big 'fly lab', at his microscope or talking with his students, with whom he had a very close personal relationship.

Patterson's early research was embryological. He studied the mechanism of development in the nine-banded armadillo, in which monozygotic quadruplets are invariably produced. From polyembryony in a mammal it was a natural step to studying polyembryony in the wasp *Paracopidosomopsis floridanus* Ashmead—a rolling name with which Patterson used to impress his elementary students, just as, in later years, he was able to silence an inquisitive Texas yokel by assuring him that his peculiar activities with an insect net were "collecting *Drosophila pseudoobscura* Frolova for my friend Professor Theodosius Dobzhansky".

Following on the discovery by Muller in 1927 of the mutagenic properties of X-rays, Patterson turned his attention to radiation genetics and worked on somatic mutation, mosaicism, gynandromorphs and the production of deletions and translocations by X-rays. But by the middle 1930's his active and restless mind seemed to have tired of these lines of work and for a while he devoted himself to building up a great collection of the flint artefacts of Texas and the neighbouring States, on which he published several papers. At last, in 1938, he found his greatest field of activity in the evolutionary genetics of *Drosophila*. This was a few years after Painter had shown that the salivary gland chromosomes of *Drosophila* could be used for an entirely new type of cytogenetic analysis which permitted a detailed comparison of the gene sequences of different species. The idea seems to have suddenly struck Patterson that he wanted to study, not just *Drosophila melanogaster*, or even the dozen or so other species that had been employed until then by a few geneticists, but the whole range of species belonging to this genus of flies—200, 500 or however many there might be (we now know there are at least a thousand).

Collecting expeditions were sent out to all parts of the United States and Mexico and later to Central America, Canada, the Caribbean and the Pacific area. Hundreds of species were brought back to the Texas laboratory, which became a living museum of *Drosophila* stocks which were subjected by Patterson and his students to a great variety of genetic techniques designed to elucidate their relationships. Painter's salivary gland technique was fully exploited in this work. The results were too voluminous to be published in the regular journals, so that they appeared in the now famous *University of Texas Publications*, generously distributed free to institutions and individuals throughout the world. Both taxonomy and genetics acquired new perspectives as a result of this work, for which Patterson received the Daniel Giraud Elliott Medal of the U.S. National Academy of Sciences in 1951 (he had been elected to the Academy in 1941). His studies of the *viridis* group of species will always remain classical examples of this kind of work.

Short of stature, direct and forthright in speech, Patterson impressed one with his energy, exuberance and whole-hearted dedication to his science. He never travelled outside North America and seldom left Texas after his middle years, when he still used to spend the summers with his family at Woods Hole and participate in the main stream of American biology. Thus he became something of a legendary personality even in his own lifetime to the many younger biologists of the eastern States and the west coast who had never met him. He had little use for intellectual subtleties, and his work deals almost entirely with the big problems open to a frontal attack. Although he made no single discovery comparable in importance with those of Muller and Painter, he has an assured place in the history of genetics and evolutionary biology. His influence on the development of the University where he taught and worked for more than half a century was very great.

M. J. D. WHITE

NEWS and VIEWS

University College of North Staffordshire : Dr. H. M. Taylor, C.B.E.

DR. H. M. TAYLOR, secretary general of the Faculties in the University of Cambridge, has been appointed principal of the University College of North Staffordshire, Keele, from October 1, to succeed the late Sir George Barnes. He will bring to the service of Keele outstanding gifts of personality and a wide range of academic and administrative interests and experience. Dr. Taylor went up to Clare College, Cambridge, in 1928, after a distinguished undergraduate career at the University of Otago, New Zealand, and he continued to distinguish himself as undergraduate and research student in Cambridge. He graduated Ph.D. in 1933 and was elected Fellow of Clare in the same year. By 1939 he had made his mark in Cambridge as University lecturer in mathematics, secretary of the Faculty Board of Mathematics, director of studies in mathematics and steward of his College, and adjutant of the Officers' Training Corps. In these and many other fields he had given proof of great organizing ability, an orderly mind, industry, and a kindly and sympathetic personality.

After war service in the Army, as an instructor at the School of Artillery, Larkhill, Dr. Taylor returned to Cambridge in 1945 as University treasurer, and was made secretary general of the Faculties in 1953. He has thus had a unique experience in administering the educational and financial affairs of Cambridge, and he has made notable contributions to solving the complex problems of post-war building programmes and the academic development of the University. Dr. Taylor is in the first rank of ski-mountaineers and is also an authority on pre-Norman Conquest churches, on which he has in preparation what promises to be a definitive work. For his contributions to the study of Anglo-Saxon architecture he has recently been admitted to the fellowship of the Society of Antiquaries. To illustrate these interests he has brought a talent for photography and draughtsmanship. Despite the heavy calls of his office, he has remained readily accessible and prompt to help any member of the University staff, at whatever level, who has sought his counsel. He and Mrs. Taylor have been generous hosts, and they will leave in Cambridge many friends who will wish well to them and to Keele under Dr. Taylor's principalship.

Geography at the London School of Economics

THE constitution of the University of London is sufficiently elastic to permit the existence of many special institutions or arrangements. For the past forty years the Joint School of Geography of King's College and the London School of Economics has so flourished as to rank as the largest honours school in Britain both in numbers of staff and students. Students registered at King's College enter for degrees in the Faculties of Arts and Science, those at the London School of Economics in Arts and Economics ; by tradition, though not by requirement, the professor at King's College specializes on the physical side, his colleague and joint head at the London School of Economics on the economic and human, but both are holders of University chairs of geography. As part of the post-war expansion of the social sciences, a third chair, primarily, though not entirely, a research chair, was created and occupied by Prof. L. Dudley Stamp during 1948–58, with the title of professor of social geography. Prof. Stamp was succeeded in the regular professorship and joint headship of the School by Prof. R. Ogilvie Buchanan, who was previously at University College, London (*see Nature*, **164**, 475 ; 1949). Prof. Buchanan retires in September under the age limit after thirteen years of office, during which he has held with distinction many positions in the University—including the present chairmanship of the Academic Council.

Prof. Emrys Jones

WHEN Prof. Stamp retired through pressure of outside work in 1958, a third chair of geography was established, to which Dr. Michael J. Wise was appointed, together with a readership in social geography to which Dr. Emrys Jones was appointed. Dr. Jones now becomes the third member of the professorial triumvirate—with Prof. S. W. Wooldridge and Prof. Wise. Although the special chair or readership in social geography is now therefore in abeyance, Prof. Jones's appointment assures that the field of study, essentially the application of geographical methods of survey and analysis to present problems, will not be neglected. Trained under Prof. H. J. Fleure at Aberystwyth, he went to London after some years at the Queen's University of Belfast. His recently published book, *A Social Geography of Belfast*, is a notable contribution, breaking new ground and showing promise of new developments in the borderland between sociology and geography.

Botany at Jodhpur: Prof. C. V. Subramanian

PROF. C. V. SUBRAMANIAN has been appointed to the newly created chair in botany of the University of Rajasthan, at Jodhpur. Prior to his appointment, Prof. Subramanian had successively held the posts of lecturer (1951–53) and reader (1953–58) in botany at the University of Madras, and professor of plant pathology (1958–60) in the Indian Agricultural Research Institute, New Delhi. After graduating with a first-class honours in botany from the University of Madras in 1944, he studied soil mycology under Prof. T. S. Sadasivan in the same University, and obtained his Ph.D. in 1947 for work on the saprophytic behaviour of the *Fusarium* causing cotton wilt. In 1957 he obtained the D.Sc. degree of the same University for his work on the taxonomy of imperfect fungi. For several years past he has made an intensive study of the hyphomycetes including soil *Fusaria*, and has published many papers on the tropical forms of this group, as well as the Sphaeropsidales which had hitherto not received much attention from Indian mycologists. For some time Prof. Subramanian worked in the Botany School, Cambridge, with Dr. S. D. Garrett on soil fungi, and in the Commonwealth Mycological Institute, Kew, on hyphomycetes with Mr. E. W. Mason. Prof. Subramanian is a Fellow of the National Institute of Sciences of India and of the Indian Academy of Sciences. Although a new laboratory has yet to be constructed at Jodhpur, work has

already been commenced by him on the taxonomy and biology of coprophilous and soil fungi, on the taxonomy, physiology and cytology of *Helminthosporium* species attacking cereals, and on abnormal growth in plants. B. Tiagi, appointed as reader, has a long record of active research in plant morphology and embryology. The Department will soon have a separate building together with a general herbarium of higher plants, a mycological herbarium and a collection of living cultures of fungi.

Ford Foundation Research Fellowships of the Zoological Society of London

In May 1960 the Ford Foundation made a grant of 550,000 dollars to the Zoological Society of London to endow three senior research fellowships and three junior research fellowships in animal reproduction. The Council of the Society has now appointed Dr. Peter A. Jewell, Dr. Lorna M. Kellas and Mr. D. R. S. Kirby to fellowships. Dr. Peter A. Jewell, who will hold the appointment for five years, is at present working at the Royal Veterinary College on the breeding biology of Soay sheep, which are confined to the Island of St. Kilda, and which present unique material for the investigation of a population of small ungulates. He also intends to study the reproductive performance, under laboratory conditions, of various forms of *Apodemus*. Until suitable laboratory space is available at the Society's Gardens, Regent's Park, Dr. Jewell will work in the Department of Animal Husbandry and Veterinary Hygiene, Royal Veterinary College, London. Dr. L. M. Kellas, who is appointed for three years, at present holds an appointment in the Department of Veterinary Histology, University of Glasgow Veterinary School. Dr. Kellas will make a histological and histochemical study of the intra-epithelial granular cell which occurs in the placenta of ruminants. She will also study the reproductive tracts of the giraffe, having already obtained certain material for these studies while on field expeditions to Central Africa. Mr. David R. S. Kirby has been appointed for a period of three years, as from October 1, 1960, and for the time being will continue to work in the Department of Zoology and Comparative Anatomy in the University of Oxford. He will study the effects of abnormal environments on the development of the embryo, with particular reference to the inhibitory influence of the endometrium on the spread of the cells of the trophoblast.

New Atomic Energy Authority Reactor

A new low-power reactor called *Vera* (Versatile Experimental Reactor Assembly) started operating for the first time at the Atomic Weapons Research Establishment, Aldermaston, on February 22. It is being used in reactor physics experiments to improve nuclear data and methods of calculation for fast critical assemblies. More information on these systems is required for many problems relating to the safety of storage and processing of fissile materials, and for the fast reactor development programme. The reactor includes a core region of thin-walled steel fuel tubes surrounded by a natural uranium reflector —the whole forming a cylinder 4 ft. high and 5 ft. in diameter. The fuel tubes are loaded with fissile and diluent material plates 1·7 in. square and $\frac{1}{8}$ in. thick. By appropriate loadings the composition and size of the reactor core may be varied to examine the nuclear importance of materials over a wide range of neutron energies. The reactor is designed to separate into two parts for safe loading, the two halves being brought slowly together by remote control. An accelerator associated with *Vera* enables neutron bursts to be generated for measurements of reactivity and time-dependent behaviour. The reactor is located in a large concrete cell which is sealed during operation. As the power will not exceed 100 W. special cooling is not required. This work forms part of a programme of experimental and theoretical nuclear data work at the Atomic Weapons Research Establishment and is co-ordinated with fast reactor work in progress at other establishments of the U.K. Atomic Energy Authority.

New British Base in the Antarctic

A new British Antarctic base—one of the most southerly in the chain of scientific stations maintained by the Falkland Islands Dependencies Survey—has been set up on Adelaide Island. Sir Vivian Fuchs, director of the Survey, states that the new base is on the east side of Adelaide Island, in approximately latitude 67° 40′ S. Adelaide Island is about 70 miles long and 30 miles wide with high mountains, the peaks of which reach 4,000–7,000 ft. The new base was established on February 3 and will enable the survey and geology of the Island to be completed, besides acting as a supply station from which men and stores can be flown to other bases. Two Otter aircraft have already arrived at Adelaide and are at present in the course of flying stores to Fossil Bluff, the site of a new station in lat. 71° 20′ S., long. 68° 17′ W. This will be the farthest south base in the Graham Land area, and from it exploratory journeys will be made in Alexander Island, a high mountainous region some 20,000 square miles in extent.

Afforestation in National Parks in Britain

In a written answer circulated in *Hansard* of February 14, the terms of a scheme for afforestation in the national parks in Britain is given, together with a letter sent by the National Parks Commission on January 26, 1961, to the individual park planning authorities recommending its adoption. The purpose of the scheme is to secure consultation of the park planning authorities on proposals for private afforestation of any land that has not hitherto been planted. The Timber Growers' Organization, the Country Landowners' Association, the Forestry Commission and the National Parks Commission are all anxious to secure that in the future use of land in national parks, proper regard should be given both to the needs of forestry and to the preservation and enhancement of the natural beauty of the landscape. To avoid conflict between these two interests, the parties to the agreement believe that the closest co-operation should be maintained between those concerned with afforestation and those responsible for accomplishing the purposes for which national parks have been established, and they agree accordingly that the Park Planning Authorities should be given the opportunity of commenting on all proposals for the afforestation of any land not hitherto planted. In each national park, except where special arrangements have already been made, it is proposed that the Park Planning Authority should carry out with the Forestry Commission a survey with the view of compiling maps classifying the land in the park so far as possible into: (*a*) areas where there is a strong presumption

that afforestation would be acceptable; (*b*) areas where, although there is a presumption against afforestation, proposals might be acceptable; and (*c*) areas where there is a strong presumption against afforestation. These categories are devised as a general guide to policy and should be adjusted where necessary to meet particular circumstances. The surveys are intended to be discussed between the planning authorities, the National Parks Commission and the other parties to the agreement. The Forestry Commission has promised to frame its afforestation proposals in accordance with the surveys, amended as necessary after these consultations, and it is hoped that private landowners will do likewise. The arrangements will not apply outside national parks, nor to the replanting of existing woodlands. The agreement does not refer to the character or type of afforestation.

Radioactive Materials in Food and Agriculture

Although the references quoted in the recent report of a Food and Agriculture Organization Expert Committee, entitled *Radioactive Materials in Food and Agriculture*, and the contamination-levels available to the Committee were no more recent than 1958, and there are still wide gaps in our information, the publication represents a valuable balanced and readable general survey of the subject, and one which lays stress on basic concepts (Pp. ix + 123. Rome: Food and Agriculture Organization of the United Nations. London: H.M. Stationery Office, 1960. 7*s.* 6*d.*; 1.50 dollars). Radionuclides enter the human body, primarily via the food chain, along which a great many environmental variables can modify the contamination of the final food product. Some emphasis has been placed here on matters of soil and plant contamination, but attention is given to animal products, food processing, marine biology, human dietary aspects and overall survey and sampling problems. Although the predominant man-produced contamination of our environment with radionuclides on a world-wide scale has its origin in nuclear explosions, effluents from nuclear power-plant can be a factor of local importance. Some attention is directed to the ability of some marine forms to concentrate certain radionuclides one-hundred-fold from the sea, and to a feasible method for decontaminating milk supplies in an emergency. The Committee makes important recommendations which specify those particular fields where further research and survey work are most urgently needed. It is perhaps as well that the few errors which occur in the text so greatly alter the sense of the passage that they are easily detected: for example, on page 41, environmental carbon-14 does not amount to approximately 10 11 per cent of carbon-12.

Origin and Evolution of Coal

The Geological Survey and Museum has published a 17-page pamphlet entitled *The Origin and Evolution of Coal* (Department of Scientific and Industrial Research. By Dr. P. J. Adams. Pp. i + 17. (London: H.M. Stationery Office, 1960.) 1*s.* 9*d.* net): this is substantially a reprint of an article that appeared in the *Fuel Economy Review* of 1955. Starting from the definition of coal as "a combustible rock which had its origin in the accumulation and partial decomposition of vegetation", it traces the history of the different vegetable ingredients that went towards the formation of coal, first through their biochemical decomposition to peat and sapropel (slimy sediment), and later through physical and chemical changes brought about by temperature and pressure during the course of the burial of peat and sapropel to greater depth. The familiar 'humic' coals, assumed to be derived from peat, together with their constituent macerals, and the sapropelic coals (cannel and boghead), are then described. Following a brief discussion of the part played in these processes by crustal movement, the lignite–anthracite series is discussed with reference to the progressive chemical changes involved. Finally, the geological record of coal formation is summarized in a useful table. Begun about 300 million years ago, this process still continues, though in small measure: for example, in the Everglades of Florida. It is thought possible that natural graphite might be derived from still earlier coals. This booklet should prove helpful to those requiring a concise picture of coal geology, for use in lecturing and teaching.

Labelling of Medicinal Preparations

A memorandum giving guidance on the procedure to be followed in devising labels and titles for compounded medicinal preparations has been issued by the Association of British Pharmaceutical Industry, the Proprietary Association of Great Britain and the Association of Public Analysts (*Labelling Procedure for Compounded Medicinal Preparations*. Pp. 6. London: Association of British Pharmaceutical Industry, 1960). Section 6 of the Food and Drugs Act, 1955, enacts certain requirements with regard to the labelling of food and drugs. When considering the provisions of the Act practitioners realize that the attitude of the public to the purchase of medicinal preparations is not necessarily identical with their approach to the purchase of food. Consequently, it may be desirable to apply to medicinal preparations labelling requirements comparable with those introduced for food by Statutory Orders and Instruments. Further, the law does not impose on medicinal preparations labelling requirements comparable with those introduced for food. The memorandum gives detailed recommendations for labelling as well as definitions of the compounds affected.

Nuclear Fusion: Journal of Plasma Physics and Thermonuclear Fusion

It is natural, though not necessarily pleasing, that the increased interest in the physics of ionized gases should lead to the appearance of specialist journals dealing with recent developments in that subject. *Nuclear Fusion*, subtitled *Journal of Plasma Physics and Thermonuclear Fusion*, which will probably be preoccupied for some time with the former subject, is the latest addition (**1**, No. 1 (September 1960). Pp. 68. Published quarterly. (Vienna: International Atomic Energy Agency, 1960.) Annual subscription 250 Schillings; 70*s.*; 10 dollars. Single issues 75 Schillings; 21*s.*; 3 dollars). It is a well-produced journal, with photographs and diagrams accompanying the text, although the advantage of two-column printing in a subject so mathematical as to require frequent whole-width displayed formulæ is obscure. The material in the first issue, which is of high quality, consists of the first part of a leisurely and complete survey of the oscillations of a plasma, a highly mathematical discussion of the stability of an axially symmetric plasma, a brief note on the energy distribution of thermonuclear neutrons,

and two experimental papers on rapidly compressed plasmas. There is the usual impressive list of editors, and, as befits the organ of an international agency, abstracts are provided in four languages, English, French, Spanish and Russian.

Ilfracombe and District Ordnance Survey Map

THE Ordnance Survey Department has published a map at the scale of 2½ in. to the mile showing the North Devon coast from Saunton Sands to Combe Martin and extending nearly ten miles inland; Lundy Island is shown as an inset (Map of Ilfracombe and District. Sheet 856. Scale: 1:25,000, about 2½ inches to one mile. Chessington, Surrey: Ordnance Survey, 1961. Paper, 6*s*. 6*d*. net). Two new features have been introduced in this publication. The sheet size has been increased from the 10-km. square, at present used for Ordnance Survey maps at this scale, to 20 km. east to west by 15 km. north to south (roughly 12½ miles by 9½ miles). In addition, to keep the price as low as possible, the cardboard cover normally used for the folded style maps has been discarded and the cover design has been printed as an integral part of the map. Covering as it does a very popular holiday and walking area, it is questionable whether the last-mentioned innovations have not, in fact, jeopardized the durability of the map, which is likely to have to stand up to some rough treatment.

Science Progress

A VALUABLE review of the giberellins by P. W. Brian, of the Akers Research Laboratories, Imperial Chemical Industries, Ltd., in the latest issue of *Science Progress* (**49**, No. 193; 1961) is accompanied by two other articles which should be of considerable interest to those wishing to extend their knowledge of genetics. Dr. G. H. Beale, of the Department of Animal Genetics, University of Edinburgh, describes recent work on the mechanics of cytoplasmic inheritance, while Dr. Gordon Haskell, of the Genetics Department, Scottish Agricultural Institute, reviews scientific advances in the past decade which are associated with the life-history and cyto-genetics of the genus *Rubus*. The journal also contains the usual sections describing recent developments in various branches of natural science, and many authoritative book reviews.

A Large Red-Shift

NEBULAR red-shifts up to one-fifth of the velocity of light have been reached by spectroscopic investigations. The absorption features in the spectra of even fainter and more distant galaxies are veiled by the night-sky spectrum. Emission lines remain visible for much fainter galaxies than absorption lines, and the detection of galaxies with strong emission lines would therefore permit spectroscopic determination of very large red-shifts. The investigation of radio sources offers a promising way of finding distant galaxies with emission lines; many of the strongest radio sources have been identified with such galaxies. Among the known radio sources one has now been identified with a galaxy of apparent magnitude 21, which appears to be the brightest member of a cluster of galaxies, and which has a spectrum showing a strong emission line at λ5448 Å. The emission line is almost certainly the forbidden doublet of ionized oxygen, the laboratory wavelength of which is 3728 Å., and the large red-shift corresponds to a velocity of 0·46 times the velocity of light (R. Minkowski, *Astrophys. J.*, **132**, 909; 1960). W. A. Baum has used photo-electric photometry to determine a red-shift of 0·44 times the velocity of light for two fainter galaxies of the cluster. There is thus every reason to believe that the first galaxy is, indeed, a real member of the cluster of galaxies. These results establish the possibility of reaching red-shifts which are large enough to permit discrimination between different cosmological theories.

Scottish Field Studies Association

RECENTLY the programme for the Scottish Field Studies Association has become available and shows a welcome expansion in the scope of its courses, of which seventeen are now being offered. The majority of the botanical courses are once more centred on the Garth Field Centre. However, other courses are being organized at: the Isle of Raasay and the Isle of Great Cumbrae (marine biology); the Isle of Arran and North Ballachulish (geology); Beinn Eighe, the Isle of Arran and Strathpeffer (zoology). Two geographical field studies are being arranged from the Garth Field Centre and in the Strathpeffer region. Fees for the courses, which in each case last a week, vary from £7 to £11 3*s*. Further information can be obtained from the Scottish Field Studies Association, 179 West Regent Street, Glasgow, C.2.

Institute of Metals

THE spring meeting and annual general meeting of the Institute of Metals are to be held at Church House, Great Smith Street, London, S.W.1, during March 21–23. The annual general meeting will be held on the morning of March 21. On each occasion the programme is divided into two sections, *A* and *B*, which will run concurrently in the Hoare Memorial Hall and the Convocation Hall, as follows: *March* 21 (*A*) compatibility problems in gas-cooled reactors, (*B*) aluminium alloys (Prof. M. Polanyi will be giving the May Lecture, entitled "Science: Academic and Industrial", in the evening); *March* 22 (*A*) copper alloys and X-ray fluorescence analysis, (*B*) the contribution of constitutional research to general metallurgical problems; *March* 23 (*A*) extrusion, (*B*) segregation to grain boundaries. Further information can be obtained from the Secretary, Institute of Metals, 17 Belgrave Square, London, S.W.1.

International Congress on Metallic Corrosion

THE first International Congress on Metallic Corrosion is to be held at the Imperial College of Science and Technology, London, S.W.7, during April 10–15. The programme has been divided into fifteen sessions which include such topics as effects of corrosion, corrosion inhibitors, corrosion protection, high-temperature oxidation, corrosion fatigue, etc. It will also include four plenary lectures: "Chemical and Electrochemical Behaviour of Metals at Passivation Ranges", by Prof. Y. M. Kolotyrkin; "Radiotracers as applied to the Study of Metallic Corrosion", by Prof. P. Lacombe; "The Advancing Frontiers of Corrosion Science", by Prof. H. H. Uhlig; "Factors deciding between Active Corrosion and Protective Film Formation", by Dr. U. R. Evans. Further information can be obtained from the Honorary Secretary, The First International Congress on Metallic Corrosion, 14 Belgrave Square, London, S.W.1.

Teyler Essay Competition

THE 1961 competition for the Teyler Prize, organized jointly by the Teyler Foundation and the Second Teyler Society, will take the form of an essay on modern theories of the genesis of organic matter and macromolecules originating during a phase of development of the Earth, prior to the appearance of the first living organisms. The Teyler Prize consists of a gold medal or 400 Dutch guilders. The closing date for the competition is January 1, 1963. Further information can be obtained from the directors of Teylers Stichting, Fundatiehuis, Damstraat 21, Haarlem (Netherlands).

University News :

Belfast

THE following appointments to lectureships have been announced : B. E. S. Gunning (botany) ; Dr. W. D. McGrath (physical chemistry) ; B. C. S. Wilson (archæology). Grants have been received as follows : from the Department of Scientific and Industrial Research, £695 for the purchase of an argon chromatograph, and £768 for the purchase of a gas chromatograph with flame ionization detector, both for research in the Department of Chemistry ; from the Wellcome Trust, £5,500 for the purchase of an Akashi electron microscope and an ultramicrotome for use in research by the Department of Zoology.

Birmingham

AMONG the recent appointments are the following : J. W. Fortey, to be lecturer in civil engineering ; D. E. N. Davies, to be Associated Television Fellow in the Department of Electrical Engineering ; B. Henderson, to be William Gibbins Research Fellow in the Department of Physical Metallurgy ; Dr. A. I. Rees to be Imperial Chemical Industries Fellow in Geophysics in the Department of Geology.

Keele

THE Nuffield Foundation has given £20,000 to the University College of North Staffordshire for the purpose of setting up and maintaining a special library, to be known as the Nuffield Library, appropriate for the foundation year of general studies in the College. This Library, to be housed in the new University Library building under construction, will contain multiple copies of a number of texts which are basic to the study of each of the twenty or more subjects which go to make up the foundation year course. Part of the grant is to be available to keep this Library constantly up to date.

London

DR. F. F. HEYMANN has been appointed reader in physics in the University of London, and Dr. J. Lewis reader in chemistry in the University of London, in respect of posts held by them at University College.

Sheffield

THE following appointments have recently been announced : Dr. S. C. R. Dennis, senior lecturer in applied mathematics ; Dr. R. C. Hewson-Brown, lecturer in applied mathematics ; Dr. D. S. Dugdale, Speedicut research fellowship in mechanical engineering ; J. Beech, United Steel Companies' fellowship in metallurgy ; D. H. Warrington, J. H. Andrew fellowship in metallurgy ; A. Mitchell, C. H. Desch research fellowship.

Announcements

PROF. J. D. BERNAL, professor of physics in Birkbeck College, University of London, has been elected a member of the Czechoslovak Academy of Sciences, in recognition of his outstanding contribution to scientific knowledge in the field of physics.

SIR THOMAS SCRIVENOR, deputy high commissioner for Basutoland, the Bechuanaland Protectorate and Swaziland, has been appointed secretary of the Commonwealth Agricultural Bureaux.

THE third meeting of the Biological Engineering Society is to be held in Bristol on April 29. The Society will be visiting the University, in particular the Department of Anæsthetics and the Burden Neurological Institute. Further information can be obtained from Dr. A. Nightingale, Physics Laboratory, St. Thomas's Hospital, London, S.E.1.

A GENERAL meeting of the Association of Applied Biologists is to be held at the Manor House, Rothamsted Experimental Station, Harpenden, on March 10. The meeting will include a symposium on "Physiology of Field Crops". Further information can be obtained from Miss G. N. Thorne, Rothamsted Experimental Station, Harpenden, Herts.

A ONE-DAY symposium on the application of interference microscopy to problems of research is to be held by the Royal Microscopical Society on March 15 in its rooms at Tavistock House South, W.C.1. Further information can be obtained from the General Secretary, The Royal Microscopical Society, Tavistock House South, Tavistock Square, W.C.1.

THE fourth symposium in agricultural meteorology will be held in the University College, Aberystwyth, on March 8. The topic for discussion is "Soil Climate with Special Reference to the British Isles". Particulars can be obtained from Mr. James A. Taylor, Department of Geography and Anthropology, University College, Aberystwyth.

THE fourteenth Laboratory Animals Centre Congress is to be held at the University of Bristol during April 10–11. Admission to the Congress is by invitation only. Forms of application and further information can be obtained from the Director, Laboratory Animals Centre, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey.

THE Third Australian Spectroscopy Conference will be held in the Chemistry School, University of Sydney, during August 22–24, under the sponsorship of the Standing Committee on Spectroscopy of the Australian Academy of Science. The Conference will cover all aspects of pure and applied spectroscopy including the newer fields such as resonance spectroscopy. Further information can be obtained from Dr. L. E. Lyons, Department of Physical Chemistry, University of Sydney.

GEOCHEMICAL LABORATORIES, LTD., 2 Elmfield Avenue, Teddington, Middlesex, announce that these Laboratories, hitherto carried on in partnership by Mr. H. B. Milner and Mr. A. H. Clarke, will be continued by Mr. Clarke under the same name. Mr. Milner will continue to be actively concerned with the Laboratories and has agreed to act as consultant and adviser.

RECENT DEVELOPMENTS IN PLANT NEMATOLOGY

THE Association of Applied Biologists held a symposium on "Recent Developments in Plant Nematology" on January 20 at the British Museum (Natural History). The symposium was well attended and appears to have been appreciated.

Dr. H. C. Gough (National Agricultural Advisory Service, Cambridge), speaking on "The Importance of Plant Parasitic Nematodes in Britain", pointed out that the root nematodes, species of *Heterodera*, are the most serious pests. *H. rostochiensis* infests at a detectable level more than 80 per cent of potato fields in Holland, Lincolnshire, and about 40 per cent in the Isle of Ely; about 10 per cent of the total potato acreage in eastern England is infested badly enough to cause serious crop loss. In the case of glasshouse tomatoes, the pest often has to be controlled by costly steam sterilization. *H. schachtii* infests about 2 per cent of the total beet-growing area, and a sugar beet eelworm order was introduced in 1943 to reduce the spread and build-up of the pest by control of cropping. Pea root eelworm *H. göttingiana* could well become a serious pest in the rapidly expanding vining pea industry. Stem eelworm, *Ditylenchus dipsaci*, is most serious on narcissus and tulips in the bulb-growing areas. On narcissus, it is controlled to a considerable extent by regular hot-water treatment, but on tulips no similar satisfactory treatment has yet been devised. Stem eelworm in oats is fairly widespread, though most prevalent in northern Britain, but losses can be prevented by the use of good resistant varieties of oats. *Aphelenchoides ritzemabosi* on chrysanthemums, always a serious potential pest, is now controlled by parathion dipping of stools and cuttings at a very low cost.

Dr. J. B. Goodey (Rothamsted) chose as his topic "Taxonomic Relatedness", and claimed that the recognition of new species has led to progress in solving some refractory problems in nematology. He illustrated this by referring to the fragmentation of the old taxa *Heterodera schachtii* and *H. marioni* into a number of recognizable species of *Heterodera* and *Meloidogyne* respectively. In *Ditylenchus* less progress has been made, for although the stem nematodes are now split into three species, *D. dipsaci* is still recognized as containing numerous 'biological races'. Work on *Xiphinema diversicaudatum*, a virus vector, shows that the standard monograph, containing the description of this species, appears to err. The variation shown by this nematode is extensive enough to suggest two possible species if only the extremes are taken, indicating the need to treat taxonomy dynamically with the study of plenty of living material. It was suggested that the taxonomist should not regard himself or others as infallible. The adequate description of new species requires the consideration of about 150 aspects of a nematode, and while to others his work might appear intuitive and subjective, his feet are kept firmly on the earth by the necessity to explain unambiguously his conclusions to sceptical colleagues.

In discussing "The Ecology of Soil Migratory Nematodes", Dr. R. D. Winslow (Rothamsted) defined these nematodes as those root-feeding members of the Tylenchida and Dorylaimoidea in which the female does not become cystic. In the soils investigated by him at Rothamsted and elsewhere *Pratylenchus*, *Paratylenchus*, *Tylenchorhynchus*, *Rotylenchus* and *Helicotylenchus* are most common, with *Pratylenchoides*, *Criconemoides*, *Hemicycliophora*, *Trophurus*, *Longidorus*, *Xiphinema* and *Trichodorus* occurring occasionally. In arable crops at Rothamsted and Woburn (Beds.) highest numbers of total nematodes and of total Tylenchida occur in late summer or autumn. Generally at Rothamsted, and in some cases at Woburn, these numbers are well maintained during winter, falling in spring to a minimum in May or June. Other factors greatly affecting nematode numbers are vegetation, soil-type and *p*H. Cereals generally support more plant-parasitic and other nematodes than do potatoes and sugar beet. Spiral nematodes are numerous in the heavy soil at Rothamsted; very rare in the lighter Woburn soil. *Pratylenchus pratensis* is associated with low *p*H on a hay-field at Rothamsted (probably due to *p*H affecting the botanical composition of the sward), whereas the fungivorous *Aphelenchus avenae* is associated with high *p*H. In forest nurseries *Hoplolaimus uniformis*, *Trichodorus pachydermus* and *A. avenae* are associated with relatively high *p*H.

Mr. F. G. W. Jones (Rothamsted) first briefly summed up the present state of knowledge of "The Orientation and Host-finding by Soil-inhabiting Plant-parasitic Nematodes" by saying that there appears to be no evidence of nematode response to *p*H gradients, and that tests on response to temperature gradients have not been made. There is evidence of response to moisture gradients, to carbon dioxide, to certain acidic oxidizing and reducing compounds, to root exudations of unknown constitution and possibly to the products of bacterial activity in the rhizosphere. Response to redox potentials and to electric currents is also known. He then described some of his own work on the behaviour of various nematodes, *Turbatrix aceti*, *Heterodera schachtii* larvae and *Ditylenchus dipsaci*, when exposed to electrical gradients. Nematodes respond to electrical gradients of more than 30 mV./mm., and, as many nematodes are about 1 mm. long, this represents a change of potential from head to tail. In a gradient of 100–200 mV./mm., *D. dipsaci*, which have been moving at random, tend to move more spasmodically and to swing their heads in a wide arc. Often, after this preliminary swinging movement, the head tends to face the cathode, followed by free swimming towards it. When the current is reversed, movement follows, leading to a reversal of the direction of swimming.

Mr. C. C. Doncaster (Rothamsted) showed a film of "Some Nematode Feeding Mechanisms". This illustrated the feeding of spear-bearing nematodes and those with open stomas. In the first group, *Aphelenchus avenae* thrusts the spear repeatedly against a fungal hypha followed by a rapid pumping action of the valve of the median bulb, thus ingesting the contents of the hypha: but in *Aphelenchoides ritzemabosi*, feeding on mesophyll cells of *Stellaria media* in a water mount, the median bulb shows only gentle pulsation while the spear is inside the cell. It was suggested that feeding in *A. ritzemabosi* may be more the tapping of cell sap under pressure. In the second group, *Diplogaster* sp., *Pelodera lambdiensis*

and *Rhabditis oxycerca* are saprophages. In *Diplogaster*, food particles are sucked in by the expansion of the tri-radiate lumen of the corpus (first bulb), which acts rather like a pipette. The lumen through the base of the corpus can be closed completely and acts as a valve. From the first bulb, food is transferred through the isthmus and second bulb by a wave of peristaltic-like action caused by successive contractions of the radial muscles surrounding the tri-radiate lumen of both parts. In *P. lambdiensis* and *R. oxycerca* the second bulb has three equally spaced valve plates which move backwards into a cup-like cavity. The whole process of feeding is very complex, but appears to be divisible into the following stages: (*a*) the procorpus and corpus open, drawing in food and, on closing, food collects in the forepart of the isthmus; (*b*) this food mass is carried further back to the valve by a wave of 'peristalsis'; (*c*) the cup behind the valve dilates, sucking the food through the valve flaps, which then flick back into the cup together with the whole of the anterior part of the valve; (*d*) the cup collapses, forcing the food into the œsophago-intestinal canal behind it, this canal also showing 'peristaltic' dilation and collapse.

Dr. H. R. Wallace (Rothamsted), in discussing "Plant Reaction to Parasitism by Nematodes", listed some of these reactions: he mentioned rounding of cells and loosening from one another, possibly by the action of pectic enzymes in tissues attacked by *Ditylenchus dipsaci*; the formation of giant cells in roots attacked by *Heterodera* spp. and *Meloidogyne* spp., possibly indicating the presence of growth hormones; cell hyperplasia and hypertrophy in roots attacked by *Radopholus similis*, and extensive necrosis associated with the invasion of roots by *Pratylenchus* spp. He went on to describe his work on the attack in chrysanthemum leaves by *Aphelenchoides ritzema-bosi*. In susceptible varieties few cells appear to be attacked, the nematodes remain very near their point of entry, and reproduction goes on; but in resistant varieties many cells are attacked, the nematodes move far and wide and there is almost no reproduction. Resistant varieties show rapid and extensive leaf discoloration associated with the enzymic oxidation of plant polyphenols, and it is suggested that there is an absence of some nutritional factor in these leaves. Dr. Wallace ended by stressing the state of our ignorance of the inter-relationships, particularly biochemical ones, of nematode parasite and plant.

Dr. R. S. Pitcher (East Malling Research Station) spoke on "Nematode Vectors of Virus Diseases", and said that it was the pioneer work of Hewitt and Raski in California that first showed the transmission of virus by nematodes. He stressed that though this work is important in its own right, it should also stimulate study of the complex inter-relationships of nematodes and other 'soil inhabiting' pathogens and their relation to the plant and its environment. Of the 'soil-borne' viruses, those that have been transmitted by nematodes could be classified as having infectivity destroyed by air-drying of soil, and while 'tobacco rattle', which is transmitted by *Trichodorus pachydermus*, has rod-shaped particles, the others have isometric particles, for example, 'fanleaf of grape', 'peach yellow bud mosaic' and 'arabis mosaic' transmitted by *Xiphinema index*, *X. americanum* and *X. diversicaudatum* respectively and 'tomato black ring' transmitted by *Longidorus elongatus*. There is a clear correlation of disease and the presence of nematodes which are all members of the Dorylaimoidea, with relatively long spears when compared with most members of the Tylenchida, none of which is known as a virus vector. The means by which virus transmission takes place is unknown and, as yet, a matter for speculation.

"Practical Problems and Recent Trends in Nematode Control" was the topic chosen by Mr. F. C. Peacock (Plant Protection, Ltd., Jealott's Hill), who said that many of the earliest nematicides which still give good service are halogenated hydrocarbons. They are generally phytotoxic and relatively volatile substances. Methyl bromide and D-D are early examples and 1,2-dibromo-3-chloropropane a more recent one. A second group of nematicides are the organic phosphates: parathion has been used for some years; more recent examples are O-2,4-dichlorophenyl-, O-diethyl phosphorothioate and diethyl pyrazinyl phosphorothioate. This group of compounds is non-volatile and relatively insoluble in water, but has high nematicidal and residual value and low phytotoxicity, albeit high mammalian toxicity. Dithiocarbamates make good soil sterilants but have high phytotoxicity; their action against nematodes is said to be due to the breakdown product methyl *iso*thiocyanate. Various sulphur compounds, such as chlorophenyl methyl rhodanine, have high phytotoxicity which is useful in seed-bed preparation, but the tetrahydrothiophene dioxides and trithiophene (occurring in *Tagetes erecta*) have low phytotoxicity. Recently the use of yellow oxide of mercury incorporated in soil has shown promise. The observation that a glycoside from *Asparagus officinalis* roots inhibits nematode attack has led to an investigation of the systemic use of maleic hydrazide and other substances, applied to leaves to prevent attack on roots either by the exudation of toxic material or the inhibition of attractive diffusates, or theoretically the preferable killing of already established parasitic nematodes. Mr. Peacock finished by stressing the need for good husbandry so that nematicides are only supplementary in function, and the need for recognizing that different nematode diseases need treatment by different nematicides.

J. B. Goodey

AREA OF RESIDENCE OF MENTAL HOSPITAL PATIENTS

ONE of the Registrar General's series of studies on medical and population subjects contains detailed statistics about the areas from which patients were admitted to mental hospitals in England and Wales during 1957. (*Studies on Medical and Population Subjects*, No. 16; "Area of Residence of Mental Hospital Patients". H.M.S.O. 15*s*. 6*d*. net.)

The addresses of patients at the time of admission have been classified according to the administrative areas in which they are situated. Separate tables are given showing, for the first time, the numbers of admissions from each county borough and administrative county and from each metropolitan borough in the County of London. Figures are given separately

for each sex and for certain age-groups and diagnoses.

Total admissions to mental hospitals during 1957 numbered 88,943, of which 48,266 (or 54 per cent) related to patients admitted to a mental hospital for the first time. Separate figures are given for total admissions (that is, first admissions and all re-admissions) and first admissions from each area and comparisons can be made on either basis. Most of the figures which follow are based on the total number of admissions and not on the number of persons admitted and do not therefore necessarily reflect differences in the proportion of persons in an area who were admitted to a mental hospital during the year.

Of the total number of admissions, 6,859 came from the County of London, while admissions from the counties of Middlesex, Kent, Essex, Surrey and Hertfordshire numbered 4,722, 3,674, 4,054, 3,214 and 1,571 respectively, giving a total of 24,094 for London and the surrounding counties. Among the counties outside Greater London, the highest numbers of admissions were of residents in Lancashire (2,947), and the West Riding of Yorkshire (2,395).

Although the volume only contains figures of the numbers of admissions, it is possible to relate these figures to the estimated populations of the areas at June 30, 1957, to give admission-rates per 1,000 population. The ten county boroughs with the highest number of admissions, with the corresponding admission-rates per 1,000 of the resident population, were as follows:

Birmingham	2,096 (1·9)	Sheffield	812 (1·6)
Leeds	1,023 (2·0)	Cardiff	761 (3·0)
Liverpool	1,005 (1·3)	Stoke-on-Trent	735 (2·7)
Manchester	836 (1·2)	Kingston upon Hull	702 (2·3)
Bristol	823 (1·9)	Bradford	622 (2·2)

Admission-rates for Lancashire and the West Riding of Yorkshire were 1·4 and 1·5 per 1,000 respectively.

Among individual metropolitan boroughs of London those having the highest rates of admission were Stoke Newington with 2·19 (144 admissions) per 1,000 and Stepney and Chelsea both with 2·8 per 1,000 of the population (274 and 144 admissions respectively).

The higher rates of admission are not concentrated in those counties with a greater degree of industrialization. For example, the rates for Staffordshire and Durham were 1·7 and 1·6 compared with 2·5 and 2·1 per 1,000 of the population, respectively, for Cornwall and Norfolk.

There were 1,553 admissions of patients stated to have no fixed abode, or 1·7 per cent of the total number admitted. Among these the number of re-admissions was 913 or 59 per cent, a figure well above the national percentage of 46. The admissions of patients normally resident outside England and Wales numbered 188 or 0·2 per cent of the total number of admissions.

Among the causes of admission, manic-depressive reaction contributed the largest proportion for England and Wales as a whole. Of the national total of 4,868 admissions due to character, behaviour and intelligence disorders, 440 were from the County of London and a further 322 were of people with no fixed abode. In London, 1,954 out of the 6,859 admissions resulted from schizophrenia (28 per cent) and 30 per cent were for manic-depressive reaction.

The proportions due to schizophrenia among the admissions from the ten county boroughs shown above were:

Birmingham	22 per cent	Sheffield	21 per cent
Leeds	14 " "	Cardiff	18 " "
Liverpool	31 " "	Stoke-on-Trent	22 " "
Manchester	38 " "	Kingston upon Hull	24 " "
Bristol	20 " "	Bradford	18 " "

By comparison, the proportions due to schizophrenia among the admissions from the predominantly rural counties of Cornwall and Herefordshire were 11 and 9 per cent respectively.

Of the first admissions for the whole country, 6,906 were reported as due to schizophrenia (14 per cent) compared with 13,902 admissions or 29 per cent for manic-depressive reaction.

COMMUNITY MENTAL HEALTH

WITH the aid of a generous grant from the Nuffield Provincial Hospitals Trust, Political and Economic Planning has recently begun a three-year study of the mental health services of Britain with particular emphasis on the subject of community care. The work is under the control of a steering group, the director of research being Dr. F. M. Martin, of the University of Edinburgh. A broadsheet, entitled "Community Mental Health Services", gives a general background to the work and shows why, and in what directions, research is necessary*.

The greater part of the research programme of Political and Economic Planning will take the form of a study of the actual operation of community mental health services in selected areas. Districts will be chosen for study primarily because they have already developed distinctive and interesting patterns of community care, such as might prove models for other areas. It is hoped that, in at least some areas, it will be possible to work in association with locally based research workers who are already interested or actively concerned in the study of mental health services. An assessment of a particular form of organization of services must take account of the statistics of patient movement, but these cannot be adequately evaluated in isolation. It will be particularly important to make some estimate of the social and personal consequences for patients and their families, of different patterns of care, and to study closely the nature of the community services provided.

In view of the wide variety of workers likely to be engaged in community care, and of the contradictory views which have been expressed on their place in the mental health services, it would be of interest to attempt some systematic analysis of the work actually performed by health visitors, psychiatric social workers, mental welfare officers, and so on. In this way it should be possible to set an analysis of professional functions against an analysis of the needs of patients and families, and to consider how effectively they can be related to one another. A comprehensive area study should also take account

* *Planning*, **26**, No. 447 (12 December, 1960): "Community Mental Health Services". Pp. 337–356. (London: Political and Economic Planning, 1960.) 2*s*. 6*d*.

of the part played by voluntary organizations and of the work of the family doctor, whose potential short-term and long-term contribution to a community-oriented mental health service has yet to be satisfactorily defined.

In the mental deficiency field, where there is a longer tradition of community care, there seems to be fewer self-conscious experiments in progress outside the hospital service. Most local authorities appear to believe that the desirable pattern of care has been fairly well worked out, and that they know at what goals they should be aiming. There is little or nothing on the mental subnormality side comparable to the research now in progress, or being planned, for the mentally ill. There may therefore be fewer opportunities for collaborative research, but it would be desirable, in areas selected for intensive study, to examine how mental subnormality services function, and how far they meet the needs of the mentally subnormal and their families.

Another issue, deeply involved in the functioning of mental health services, is that of public attitudes towards mental disorders. The beliefs and attitudes which are, in fact, prevalent in different segments of society must inevitably influence the way in which mental health services function. They are likely to affect what is defined and recognized as 'mental illness,' to condition the response of families to illness in one of their members, and to influence both the demand for treatment and the post-hospital resettlement of former patients. There have not been many systematic studies of attitudes towards mental disorder; but it seems that the structure of such attitudes is, in fact, complex, that their psychological roots are deep, and that they have an important irrational component. It may be profitable to consider undertaking certain limited studies of attitudes and beliefs, possibly in the areas chosen for general investigation. The studies may be confined, in the first instance, to the close relatives of psychiatric patients, and to certain professional groups having special responsibilities for the care of the mentally disordered.

The scope of Political and Economic Planning's inquiry will depend on the degree of collaboration with other workers, and on the extent to which further resources may become available. There is every reason to hope that even a modest set of operational studies of the work of the mental health services may make a useful contribution to the further development of community care.

THE HYDROCHARITACEÆ IN NEW ZEALAND

ONE member of the tribe Anachritew of the family Hydrocharitaceæ, *Elodea canadensis*, has long been established in New Zealand and is now well known and widespread. R. Mason, of the Botany Division, Department of Scientific and Industrial Research, Christchurch, has now collated information from recent expeditions about this and other species in the family (*New Zealand J. Sci.*, **3**, No. 3; September 1960).

E. canadensis has not been as aggressive or so fast-spreading in New Zealand as in Britain, in spite of its initially rapid spread in New Zealand. Cheeseman (1920), when recording it for Featherston, said, "Considering how rapidly this plant increased when first introduced into Britain, it is somewhat remarkable that its spread in New Zealand has been slow since its first introduction in 1870". In 1906, 38 years after its introduction, Cheeseman had only three listed districts, Mongonui, the Bay of Plenty, and the Canterbury Plains. In 1922 Thomson said it "is now abundant throughout New Zealand". "Judging by its distribution as known at present, if Cheeseman perhaps understated the extent of its distribution, Thomson overstated it". As New Zealand conditions are different from those in Britain or Europe in many ways, the behaviour of this plant would be expected to differ. In New Zealand *E. canadensis* would have met more vigorous competition from watercress than in Britain, for watercress had been introduced in New Zealand less than twenty years before and "it immediately spread aggressively and grew to an immense size far exceeding anything seen in Great Britain".

It is not known how abundant *Egeria densa* was in the Waikato when it was first collected there in 1946, but to-day it seems the commonest weed in the river from Rangiriri downstream as far as fresh water aquatics go—some 35 miles or so. In 1958, large beds of the weed were found wherever the river was examined; the weeds reached the surface along the river edges and formed submerged weed beds well into deeper waters. In Whangape Lake, it was found to form broad beds a short distance off-shore, apparently stretching all the way around the edge.

In Waihou River, where it was found in November, 1959, it seemed to be scattered in patches rather than in large-size, continuous beds.

In 1950, when *Lagarosiphon major* was found in New Zealand, it almost covered the bed of the Waiwhetu Stream in its lower reaches above tidal influences. According to A. P. Druce it is still abundant and is mixed with *Elodea canadensis*. Druce also recently found it in a cut-off of the Hutt River behind Barton's Bush, about 8½ miles from Woburn, the nearest previously known station.

In Lakes Rotorua, and in Hamilton Lake, growth of this weed is sufficiently great to interfere seriously with fishing, boating and swimming. At Rotorua the position has become so alarming that a special committee, including representatives of the Departments of Agriculture, Lands and Survey, Internal Affairs and the Marine Department, has been formed to tackle the problem of controlling and destroying the weed.

The weed has only recently begun to grow with such vigours, although it has been present in the Lake for a long time. It has been suggested that aerial top dressing in the district has suddenly increased the fertility of the Lake water; it is far more likely that the less-vigorous *E. canadensis* has been present for many years and that *L. major* is a much more vigorous newcomer attracting attention.

Mason also describes the establishment and means of distribution of all three species.

CHOICE OF TREE SPECIES

A PUBLICATION on forestry issued by the Food and Agriculture Organization tends to make one ask: "What has forestry to do with food and agriculture?" In the introduction to a recent Forestry Development paper entitled *Choice of Tree Species**, we are told that it is a contribution to the general *World Forest Planting Manual*, about which it gives no more information. One next asks: For whom is this work intended? Its primary object is stated to be to summarize what is known about the factors which should guide the practising forester in reaching a decision about the choice of species. The second object is said to be to stimulate foresters to amplify and correct the often inadequate information presented in this book. With regard to the first object it must be said right away that the summary is extremely faulty in respect both of the completeness of the information and of the manner of its treatment. With regard to the second object, this seems to imply that the aim of a publication is not to furnish information but to ask for information.

This type of publication is a feature of the present day. The setting up and staffing—at considerable expense—of global organizations from above downwards instead of building them on well-founded services from below upwards lead to attempts being made to produce text-books intended to be of universal use. The time has not yet come when natural agencies will have reduced the face of the globe to one monotonous landscape. Perhaps in no other field is there a greater variety of working conditions than in forestry. As the author, or authors, say (p. 69), "It is, of course, quite impossible to suggest general rules on the selection of species and sites for production which would be applicable in all circumstances". Nevertheless, they have attempted the impossible. Then again (p. 170) it is admitted that "The information available from different parts of the globe is so variable that uniform presentation is not possible". Uniform presentation has not been achieved. There are very serious gaps in the sources consulted, especially in respect of European countries; some works in English on the subject have been overlooked; recent developments in the study of the major site factors are unrecorded; conclusions are accepted and illustrations reproduced from examples of plantations too young to have proved their suitability; there is a lack of discrimination in assessing the relative importance of the many publications quoted; there is a very evident bias in the selection of material and too narrow an outlook on this extremely difficult problem.

The fact is that it would be unwise to recommend to any practising forester that he should purchase and consult this book—or any book of such a global type; it would be far better that he should be advised to consult the literature available in respect of the narrower field with which he is concerned, or of areas like it. To help him in this, all that is required is information on the literature referring to his conditions, to furnish which is the task—admirably performed—of the Commonwealth Forestry Bureau, Oxford.

The age of the superman has not yet arrived. No one is qualified to undertake satisfactorily such a tremendous task as that attempted in this case. The eyes of a fool are in the ends of the Earth. It was unwise of the Food and Agriculture Organization to sponsor this book, and one can only offer sympathy to those who were enticed into wading through a vast amount of heterogeneous literature to produce it. It is understood that the Organization is assisting with forestry publications dealing with certain restricted geographical regions. This is more rational and should prove more useful.

If one is eclectic and chooses the parts of special interest to oneself, there is something of value to be had from the book. Part 3, for example, consists of monographs on four widely differing species—Norway spruce, Monterey pine, teak and blue gum, which demonstrate effectively the wide differences among tree species which render difficult the writing of a global text-book. M. L. ANDERSON

* Food and Agriculture Organization of the United Nations. FAO Forestry Development Paper No. 13: *Choice of Tree Species*. Pp. xi+307. (Rome: Food and Agriculture Organization of the United Nations; London: H.M. Stationery Office, 1960.) 17*s.* 6*d.*; 3.50 dollars.

ENERGY-LINKED CYTOCHROME OXIDATION IN MITOCHONDRIA

By PROF. BRITTON CHANCE

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THE study of succinate-linked reduction of pyridine nucleotide in mitochondria was begun some time ago[1]. More recent work demonstrates that reduction of diphosphopyridine nucleotide in mitochondria is an energy-linked reaction having a definite requirement for internal high-energy intermediates[2] or for adenosine triphosphate itself[3]. Although previous attempts to demonstrate a requirement for adenosine triphosphate failed[3], these recent experiments demonstrate the possibility of driving electron transfer reactions in the respiratory chain in reverse by means of high-energy intermediates, and it has been of interest to determine whether or not cytochrome reduction induced by substrate could be reversed by adenosine triphosphate, a possibility that is particularly attractive in connexion with theories of active transport[4,5] and photosynthesis as well. (Lundegårdh[6] has

reported an effect of adenosine triphosphate (and fumarate) on the interaction of cytochromes *b* and *dh* in anaerobic wheat roots, cytochrome *dh* being "turned over into a state of strong reduction under the influence of adenosine triphosphate (and fumarate) simultaneously with cytochrome *b* remaining more oxidized". The interpretation of this interesting result is rendered ambiguous by the fact that the existence of cytochrome *dh* in wheat roots and other plant or animal tissues has not been confirmed by other workers[7] nor by us using liquid-nitrogen spectroscopy of wheat root mitochondria (B. Chance and W. D. Bonner, jun., unpublished observations).)

The present article reports that addition of adenosine triphosphate causes the oxidation of cytochromes of mitochondria in the presence of dithionite or terminal respiratory inhibitors such as cyanide or sulphide. Stoichiometric and kinetic results indicate that this is a fairly efficient reaction; inhibitor studies suggest more than one site of interaction of adenosine triphosphate with the respiratory chain. The relationship of these results to the responses of cytochromes to adenosine diphosphate[8] and to the adenosine triphosphatase activities of mitochondria are discussed. It is apparent that the oxidation-reduction states of the cytochrome, flavoprotein and the pyridine nucleotide components of the respiratory chain are as well controlled by the adenosine triphosphate and adenosine diphosphate + inorganic phosphate-levels as by reductant and oxidant.

Preparations. Pigeon heart mitochondria were prepared by a procedure developed in this laboratory (Chance, B., and Hagihara, B., in *Proceedings of the Fifth International Symposium of Biochemistry*, in preparation) involving the use of *B. subtilis* proteinase. With succinate as substrate such mitochondria have respiratory control ratios >3 (usually 4–5) and P/O values of 1·8 with respiratory activities corresponding to a turnover number of cytochrome *c* of 6 sec.$^{-1}$ at 26°. Freshly prepared rat liver mitochondria[9] and 'digitonin particles'[10] were also used. (Thanks are due to Mr. K. Kaminker and Miss H. Diefenbach for pigeon-heart preparations and to Dr. U. Fugmann for 'digitonin' preparations.) The reaction medium was free of phosphate and magnesium and consisted of 0·27 *M* mannitol, 0·03 *M* sucrose and 0·01 *M tris* pH = 7·3. The temperature of the experiments was 26°. The cytochrome *c* concentration under the conditions of the experiment ranged from 1 to 2 μM.

The double-beam spectrophotometer[11] set at appropriate pairs of wave-lengths for cytochrome components was used simultaneously with a recording fluorometer for measuring pyridine nucleotide reduction. The latter employed 365 mμ for excitation and 450 mμ for recording[12], these wave-lengths being obtained by appropriate filters.

The split-beam spectrophotometer was used at room and liquid-nitrogen temperatures to identify cytochromes affected by the addition of adenosine triphosphate. The optical path-length was 1 mm. at low temperatures. The 'trapped steady state' method[13] was used.

Cytochrome Oxidation in the Presence of Sodium Dithionite

Although cytochrome oxidation is observed on addition of adenosine triphosphate in the presence of terminal respiratory inhibitors, there is the remote possibility in such experiments that adenosine triphosphate might somehow have interfered with the action of the inhibitor and have induced a cytochrome oxidation that was linked with oxygen and not with adenosine triphosphate. In experiments with dithionite, controls were carried out to indicate that an excess of dithionite was added so that the subsequent addition of adenosine triphosphate to the solution did not stir in sufficient oxygen to exhaust the added dithionite. This was done by titrating the dithionite solution with oxygen by means of the platinum microelectrode.

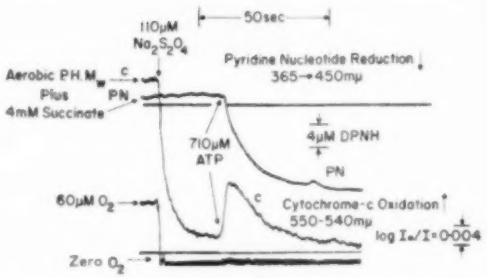

Fig. 1. Oxidation of cytochrome *c* and reduction of pyridine nucleotide caused by the addition of adenosine triphosphate to anaerobic pigeon heart mitochondria treated with dithionite, suspended in mannitol–sucrose–*tris* medium (1·9 mgm. protein/ml.). Concentrations of reactants added and the absorbancy and the concentration scales are indicated on diagram (Exp. 1936).

An experiment typical of this work is indicated in Fig. 1. Aerobic pigeon-heart mitochondria (essentially free of endogenous substrate) are treated with 4 m*M* succinate and cytochrome *c* is recorded spectrophotometrically, an upward deflexion of the trace corresponding to an oxidation. Pyridine nucleotide reduction is measured fluorometrically; a downward deflexion of the trace corresponding to increased fluorescence and increased reduction of pyridine nucleotide. The initial oxygen concentration of the suspension was diminished by bubbling nitrogen through the reaction medium, so that a value of 60 instead of 240 μM is obtained. The dithionite solution calibrated as described above is added to a final concentration of 110 μM in oxygen equivalents and causes an abrupt decrease of the oxygen concentration to zero, as indicated by the fall of the platinum electrode trace. At this time there is a rapid reduction of cytochrome *c*. There is no reduction of diphosphopyridine nucleotide, verifying that these mitochondria are free of substrate capable of directly activating reduction of this substance. As soon as the anaerobic steady state is obtained, an excess of adenosine triphosphate is added (710 μM), and there is an abrupt oxidation of cytochrome *c* and a reduction of pyridine nucleotide, the rates being respectively 0·42 μM iron/sec. and 1·2 μM reduced diphosphopyridine nucleotide/sec. The oxidation of cytochrome *c* is transitory and its reduction soon follows, the half-time for the cycle of oxidation and reduction of cytochrome *c* being about 15 sec. The reduction of pyridine nucleotide proceeds exponentially to completion, and no re-oxidation of this component is observed. This experiment indicates that the addition of adenosine triphosphate to anaerobic mitochondria causes an abrupt cyclic oxidation of cytochrome *c* and a simultaneous reduction of diphosphopyridine nucleotide.

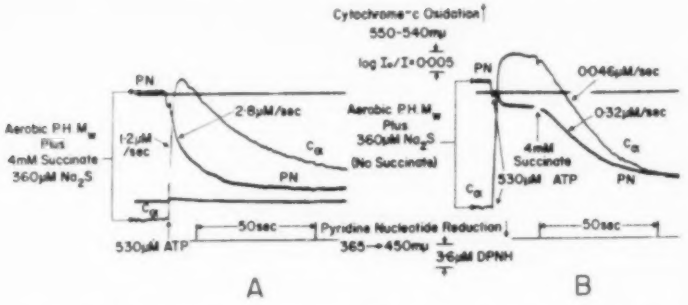

Fig. 2. Oxidation of cytochrome *c* and reduction of pyridine nucleotide in pigeon heart mitochondria inhibited with 360 μM sulphide. Left, in the presence of succinate and, right, in the absence of succinate. Concentrations, absorbancy calibrations and time scales are included in the figure. Mannitol–sucrose–*tris* medium, 1·1 mgm. protein/ml. Temperature, 26° (Exp. 1856-3)

Cytochrome Oxidation in the Presence of Terminal Respiration Inhibitors

Results similar to those of Fig. 1 have been obtained in the presence of excess cyanide or sulphide. An example of the latter is illustrated in Fig. 2*A*. In this case the mitochondria are pretreated with 4 mM succinate and 360 μM sodium sulphide. This causes complete reduction of cytochrome *c* but negligible reduction of pyridine nucleotide. On the addition of 530 μM adenosine triphosphate, there is an abrupt oxidation of cytochrome *c* at a rate of 1·2 μM iron/sec. and a corresponding reduction of diphosphopyridine nucleotide at a rate of 2·8 μM/sec. The maximal rate of oxygen utilization in the absence of sulphide and in the presence of phosphate + adenosine diphosphate (state 3) is 4·8 μM/sec. in 2-equivalent units. Thus the rate of electron transfer elicited by addition of adenosine triphosphate is high. Similar results are obtained with rat liver and brain mitochondria and with 'digitonin particles'.

As in the case of the mitochondria treated with dithionite, the cytochrome oxidation is cyclic, although longer-lived. Further additions of adenosine triphosphate cause smaller cyclic responses of the cytochromes.

Substrate Requirements for Pyridine Nucleotide Reduction and Cytochrome Oxidation

In Fig. 2*B* the experiment shown in Fig. 2*A* is repeated without succinate. There is a slow reduction of cytochrome *c* on addition of sulphide due to traces of endogenous substrate. Here the addition of adenosine triphosphate causes an abrupt oxidation of cytochrome *c* to a higher level than was obtained in the presence of succinate. Pyridine nucleotide shows only a small reduction compared with that obtained in material treated with succinate; only 20 per cent is reduced. Addition of succinate to the material treated with adenosine triphosphate allows reduction of pyridine nucleotide to proceed to the same extent that was observed in Fig. 2*A*. At the same time, cytochrome *c* reduction proceeds, but at a slower rate than the rate of pyridine nucleotide reduction. This record confirms the previous results, suggesting a specific requirement for succinate in energy-linked reduction of diphosphopyridine nucleotide[3].

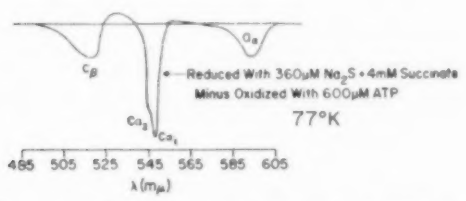

Fig. 3. Low-temperature 'trapped steady state' of oxidation of cytochromes *c* and *a*. Pigeon heart mitochondria treated as indicated in the figure, 1·2 mgm. protein/ml. Optical path 1 mm. (Exp. 1856-6)

Effect upon Other Cytochromes

To determine that a cytochrome oxidation has definitely occurred and to identify other cytochromes affected by addition of adenosine triphosphate, the 'trapped steady state' method of low-temperature spectroscopic observations has been employed in which the material in both cuvettes of the split-beam recording spectrophotometer is pre-treated with 360 μM sodium sulphide and 4 mM succinate. Just prior to freezing, 600 μM adenosine triphosphate is added to one of the cuvettes, and the spectrum representing the difference in absorbancy between the two is plotted in Fig. 3. In the interval (about 15 sec.) between addition of adenosine triphosphate and freezing, absorption peaks corresponding to cytochromes *c* and *a* have disappeared, the α_1 and α_2 peaks of the former being clearly identified. No indication of cytochromes c_1 or *b* is given in this record, and it may be presumed that directly on addition of adenosine triphosphate their oxidation states have not been measurably altered.

Time-Course of Cytochrome Change

To determine the time-sequence of the oxidation and reduction of cytochromes *c* and *a*, and to determ-

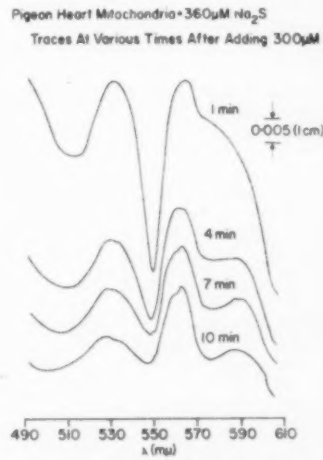

Fig. 4. Room temperature difference spectra showing the time course of the changes in oxidation- and reduction-levels of cytochromes *a*, *c* and *b*. Experimental conditions similar to those of Fig. 2*B*, 1 cm. optical path (Exp. 185c-3)

ine whether or not any slow effects on cytochrome *b* can be observed, we have recorded (Fig. 4) in the split-beam spectrophotometer room temperature difference spectra at three-minute intervals after adding 300 μM adenosine triphosphate to mitochondria treated with 360 μM sodium sulphide (succinate being omitted, cf. Fig. 2*B*). In accordance with the results of Fig. 3, the record shows clearly the oxidation of cytochromes *c* and *a* as indicated by the disappearance of absorption peaks at 550 mμ and at 605 mμ. Since this record was traced at about 1 min. after adding adenosine triphosphate, there already appears a distinctive peak at approximately 560 mμ. After a 4-min. wait, it is observed that the oxidation of cytochrome *c* is considerably smaller, as is that of cytochrome *a*. In fact, at the end of the fourth recording, the oxidation of cytochromes *c* and *a* has subsided almost completely. The spectroscopic effect in the region of cytochrome *b* has developed and a distinct peak indicating reduction of cytochrome *b* has appeared. This peak is broad and suggests the oxidation of more than one component.

Stoichiometry of Adenosine Triphosphate-Cytochrome Reaction

In view of the considerable interest in adenosine triphosphate-driven production of electron transfer for the purposes of active transport, the stoichiometry between adenosine triphosphate and cytochrome oxidation is relevant. Fig. 5*A* illustrates the titration of cytochrome *c* oxidation with adenosine triphosphate in the absence of succinate, and it is seen that a plateau is reached with less than 10 μM adenosine triphosphate. The titration curve is sigmoid, as if some other substances were being titrated prior to cytochrome *c*, or as if a certain redox potential were required. However, a stoichiometric relationship for adenosine triphosphate and cytochrome *c* is taken from the steepest part of the curve, which corresponds to 3 molecules of adenosine triphosphate per cytochrome *c*. Since cytochrome *c* is only one of four components observed to be oxidized simultaneously, the adenosine triphosphate/electron value is approximately 1. This value corresponds fairly well with the value of adenosine triphosphate/reduced diphosphopyridine nucleotide of 1·8–2·7 for reduction of diphosphopyridine nucleotide in mitochondria treated with succinate[3]. If the total adenosine triphosphate added is divided by the total electron equivalents found in cytochromes *c*, *a* and a_3 and flavoprotein, then the ratio is larger; 5·6 μM adenosine triphosphate gave a total of only 1·5 one-electron equivalents oxidized, presumably due to the sigmoid nature of the titration (Fig. 5*A*).

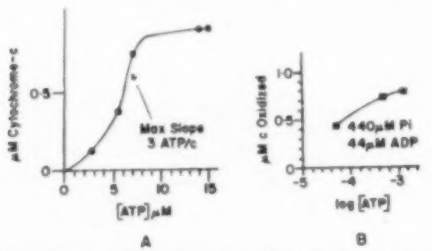

Fig. 5. Titrations of cytochrome *c* of mitochondria treated with sulphide (no succinate added) under conditions to determine an adenosine triphosphate/cytochrome 'stoichiometry' (part *A*) and an 'equilibrium' (part *B*). In the latter case phosphate and adenosine diphosphate are present. The total cytochrome concentration ($c + c_1$) was 1·2 μM in part *A*, 1·3 μM in part *B*; 360 μM sodium sulphide, 26°, mannitol–sucrose–*tris*-medium, pH = 7·4 (Exps. 198*b*, 203)

Nucleotide Specificity of the Reaction

In order to determine whether there is absolute specificity for adenosine triphosphate, we have tested the effect of various nucleotides on pigeon heart mitochondria that have been treated with succinate and sulphide as in the previous experiments. The addition of the 5′-triphosphates of ribosyl guanine, uracil, hypoxanthine and cytosine (72 μM) gives no response (less than 1 per cent), whereas adenosine triphosphate causes changes observed in Fig. 2*A*. This result is in accordance with the specificity of oxidative phosphorylation for adenosine diphosphate[14], but differs from the specificity of adenosine triphosphatase stimulated by dinitrophenol and magnesium[15].

Effects of Adenosine Diphosphate, Inorganic Phosphate and Magnesium, etc.

Experiments similar to those of Fig. 2*A* show that both adenosine diphosphate and phosphate inhibit the rate and extent of the reaction, adenosine diphosphate being considerably more effective than phosphate—an expression of their relative affinities in oxidative phosphorylation. A combination of adenosine diphosphate and phosphate is much more inhibitory, as would be expected from equation 1 (see later). It is possible to titrate cytochrome *c* with adenosine triphosphate in the presence of adenosine diphosphate and inorganic phosphate under the conditions of Fig. 2*B* (no substrate added) and an experiment on this point is given in Fig. 5*B*. It is seen that 50 per cent oxidation of cytochrome *c* can be obtained with a ratio [ADP] [*Pi*]/[ATP] of roughly 100, suggesting that in the absence of added substrate, oxidation of cytochrome *c* is not difficult to 'drive'. Magnesium is inhibitory and 0·7 mM magnesium largely blocks the effects of 32 μM adenosine triphosphate under conditions similar to those of Fig. 2*B*, presumably by activation of an adenosine triphosphatase that competes with the cytochrome reaction.

Dinitrophenol (4·5 μM) inhibits cytochrome-*c* oxidation by 50 per cent. Oligomycin (1 gm./ml.) inhibits completely. Thus the energy transfer pathway by which ATP activates reversed electron transfer is identical to that by which ADP is phosphorylated to ATP.

Effect of Ageing

Ageing of the mitochondria to the extent that respiratory control is impaired causes a considerable inhibition of the rate and extent of pyridine nucleotide reduction and of cytochrome oxidation. The cycle of oxidation and reduction of cytochrome *c* caused by the addition of adenosine triphosphate is considerably shorter, suggesting that the latter is expended not only in an energy-conserving reaction of diphosphopyridine nucleotide reduction and cytochrome oxidation, but also in the dissipative reaction involving hydrolysis of adenosine triphosphate.

Correlation with Adenosine Triphosphatase Activity

Simultaneous measurements of breakdown of adenosine triphosphate upon its addition to mito-

chondria treated with succinate and sulphide have been made by *p*H measurement[16] (unpublished work in collaboration with Drs. Saris and Ito) in order to determine the time relationships of adenosine triphosphate breakdown and the cytochrome and pyridine nucleotide kinetics. It has been found that the breakdown of adenosine triphosphate under these conditions begins at the same time as the oxidation of cytochrome and the reduction of pyridine nucleotide. It is further observed that the molar rate of breakdown of adenosine triphosphate somewhat exceeds the maximal rate of reduction of pyridine nucleotide. The rates of breakdown of adenosine triphosphate under these conditions have been compared with those observed in the dinitrophenol-activated breakdown of adenosine triphosphate and are found to be one-half to one-third the maximal rate observed. These results do not identify the pathway of breakdown of adenosine triphosphate in adenosine triphosphatase activity with the pathway of adenosine triphosphate utilization in cytochrome oxidation at the present time.

Effects of Inhibitors of Electron Transfer

Since adenosine triphosphate can interact with pairs of respiratory enzymes and does not require electron transfer through the whole chain, the effects of inhibitors on reversed electron transfer differ from those on oxidative phosphorylation obtained by electron transfer through the complete chain. Amytal, quinoline-N-oxide, and antimycin *A* slow the responses of the carriers to adenosine triphosphate, but do not eliminate slow cyclic responses of cytochromes *a* and *c*. Flavoprotein and reduced diphosphopyridine nucleotide respond to the initial addition of adenosine triphosphate (see Fig. 6), but after several further additions of the latter, the response of these components becomes negligible, pyridine nucleotide being completely reduced. In the system blocked with quinoline-N-oxide or antimycin *A*, the rate of cytochrome oxidation is so slow that electron transfer through the inhibited site to an electron acceptor such as ubiquinone is a possibility.

The oxidation of flavoprotein and the reduction of pyridine nucleotide in the system blocked with quinoline-N-oxide would appear to indicate an interaction site for adenosine triphosphate between flavoprotein and pyridine nucleotide.

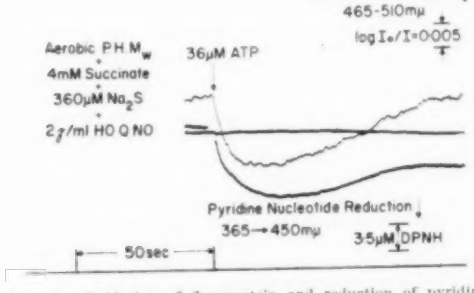

Fig. 6. Oxidation of flavoprotein and reduction of pyridine nucleotide caused by addition of adenosine triphosphate to pigeon heart mitochondria inhibited with sulphide and quinoline-N-oxide (HOQNO) under conditions similar to those of Fig. 2. Time, absorbancy, and concentration scales indicated on figure, 1·2 mgm. protein/ml. (Exp. 178)

Discussion : Relation to Active Transport and Photosynthesis

The results presented here indicate that specific oxidation-reduction reactions are induced by the addition of adenosine triphosphate to mitochondria devoid of oxidase activity due to removal of oxygen by sodium dithionite or due to respiratory inhibition by sodium sulphide. This reaction constitutes a genuine conversion from adenosine triphosphate to electron transfer, a process that has been sought for a number of years. However, it was apparent that the energy-linked reduction of diphosphopyridine nucleotide[2,3] would be accompanied by an energy-linked oxidation, provided suitable experimental conditions were found. The appropriate conditions are simple : electron transfer proceeds rapidly in the reverse direction in mitochondria that are relatively free of magnesium, adenosine diphosphate and inorganic phosphate. This discovery may be of considerable importance to our understanding of the function of the respiratory chain, and to our consideration of new ways in which metabolic processes could be affected by the transfer of the energy of adenosine triphosphate to oxidation-reduction equivalents.

It is useful to consider, on the basis of these results, the appropriate conditions for reversed electron transfer in the living cell. In intact mitochondria in anaerobiosis, a high 'phosphate potential' (see below), generated by glycolytic activity, could cause appreciable reduction of mitochondrial diphosphopyridine nucleotide and oxidation of either succinate or of cytochrome as indicated by Fig. 5*B*. A 'phosphate potential' of a few thousand calories produces considerable oxidation of cytochrome in substrate-free mitochondria (see below). For portions of the electron transfer system, such as those postulated for active transfer[6], anaerobiosis would not be required, only an appropriate 'phosphate potential'. It is apparent that the stoichiometry of the conversion from adenosine triphosphate to electrons is not yet sufficiently favourable to merit serious consideration of the mitochondrial process as an explanation for the very high efficiency observed in gastric secretion under certain conditions[6], although the principle of conversion of the energy of adenosine triphosphate to electron transfer is proved. However, in mitochondria we would not expect a ratio of adenosine triphosphate/electron exceeding that of the phosphorylation efficiency. Our stoichiometric data (~ 1 ATP/Fe) may give a low value because a portion of the adenosine triphosphate may be (1) used to affect other carriers that are oxidized and (2) split directly without its utilization in cytochrome reactions (see later).

The response of cytochromes of photosynthetic bacteria to illumination is characteristically an oxidation of cytochrome[17,18], and in some circumstances a reduction of pyridine nucleotide[19,20]. Up to this point, it has been considered that such responses are direct consequences of the effect of the photochemically produced oxidant and reductant on a series of electron-transfer carriers. The results given here make it necessary to distinguish by further experimentation between the present hypothesis and the possibility that high-energy intermediates, produced in light-induced energy-conservation reaction, could indirectly influence a chain of electron-transfer carriers in the manner illustrated by these experimental results (cf. Fig. 2). One way of distinguishing in favour of a direct effect

is by observation of cytochrome oxidation at liquid-nitrogen temperatures[22].

The phenomenon of 'water splitting' by cytochrome a_3 oxidized by adenosine triphosphate would not be unexpected in further investigations; so far we have observed that a considerable disappearance of absorption at 445 mμ occurs on addition of adenosine triphosphate to the dithionite-treated material, and is followed by a reappearance of this absorption band. It is possible that the reduction of cytochrome oxidized by adenosine triphosphate could be attributed in part to a 'water-splitting' reaction, as well as to the exhaustion of added adenosine triphosphate.

Oxidations in the Presence of Dithionite

It is remarkable that cytochrome oxidation induced by adenosine triphosphate can be observed in mitochondria in spite of the reducing power of sodium dithionite. Two explanations may be considered: (1) that adenosine triphosphate can oxidize cytochromes against the negative potential of dithionite; or (2) that dithionite does not penetrate the mitochondrial membrane (assuming that none of the cytochromes is accessible on the outside membrane of the mitochondria). In the case of the second alternative, it might be expected that no responses to adenosine triphosphate would be observed at longer times following the addition of dithionite. We have been able to observe the response to adenosine triphosphate after incubation of the mitochondria with dithionite for one and a half minutes. The lack of dithionite sensitivity recalls experiments on the light-induced oxidation of cytochromes of *R. rubrum* in the presence of a considerable excess of dithionite[23]. At the present time, we are inclined to favour explanation 2 in both cases, namely, that dithionite is acting exclusively as an oxygen absorber and not as a specific reductant of cytochromes.

Nature of the Electron Acceptor

While it is clear from Figs. 1, 2 and 3 that cytochromes are oxidized, it is important to consider the electron acceptor for this oxidation reaction. (Obviously either electrons or hydrogen atoms could be transferred.) In Fig. 2*A* the rates of cytochrome oxidation and pyridine nucleotide reduction indicate that diphosphopyridine nucleotide may be accepting about half its electrons from cytochrome oxidation, and that the remainder arise (1) from succinate oxidation or (2) from entry of adenosine triphosphate at another point in the respiratory chain to oxidize flavoprotein and ubiquinone. It is possible that both reactions occur. It is of special interest to note that in the absence of added succinate, only 30 per cent of the pyridine nucleotide is reduced, and in this case the electrons are presumably all from oxidations induced by adenosine triphosphate of other carriers. The fact that only a part of the pyridine nucleotide can be reduced by electrons transferred from adenosine triphosphate-induced carrier oxidation or from treatment of the mitochondria with a diphosphopyridine nucleotide-linked substrate[2] underlines the specific role of succinate in the reduction of the majority of mitochondrial diphosphopyridine nucleotide and supports the ideas of chemical or compartmentation differences of mitochondrial pyridine nucleotide[2].

In the absence of succinate, pyridine nucleotide can still act as an electron acceptor, although some other substance may be involved. Comparing the total of oxidized cytochromes and flavoprotein with the extent of reduction of pyridine nucleotide, more oxidized than reduced substances are found on a mole basis (1·5 : 1). However, the assay procedures should be refined, particularly that for ubiquinone, since absorption of adenosine triphosphate interferes with its assay by the spectrophotometric method[24].

The reaction kinetics of cytochromes *c* and *a* are of interest in contrast with those of pyridine nucleotide; the former resembles those of an enzyme substrate intermediate, the latter that of a product of an overall reaction. As indicated above, the difference in these kinetics is probably due to the fact that succinate supplies electrons for the reduction of a portion of diphosphopyridine nucleotide.

Speed of the Reaction

The speed of cytochrome oxidation caused by addition of adenosine triphosphate is fairly high, as illustrated by Figs. 1 and 2, but it is nevertheless only about 10 per cent of the rate of oxygen utilization obtainable in the phosphorylation of adenosine diphosphate (state 3) in pigeon-heart mitochondria. It can then be understood why the accumulation of adenosine triphosphate does not slow down respiration in oxidative phosphorylation, or at least change the state of the carriers[3,25]. In addition, phosphate + adenosine diphosphate inhibit the reverse reaction[26]:

$$\mathrm{ADP} + \mathrm{P_i} + X \rightleftharpoons \mathrm{ATP} + X \qquad (1)$$

Similarly, oxygen itself, which produces a high degree of oxidation of the carriers, inhibits the reverse reaction.

Thermodynamic Aspects

While the records of Figs. 1 and 2 show clearly that the system is not in equilibrium because of breakdown of adenosine triphosphate, it is of great interest to learn something of the [ADP] [P_i]/[ATP] values that are involved in the cytochrome oxidation. In Fig. 5*B* a preliminary value of 10^2 for half-oxidation of cytochrome *c* is obtained. If succinate is added, the value is greatly decreased, as would be expected from the increased reducing power. While conversion of these values to calories may not be meaningful, cytochrome *c* is half-oxidized in the absence of succinate at an [ADP][P_i]/[ATP] value corresponding to 3 kcal.

That some oxidation of cytochrome and some reduction of diphosphopyridine nucleotide can be observed under these conditions requires an explanation. While it is not the purpose here to present a comprehensive theory, it is suggested that a possible explanation for the oxidations and reductions over such a wide range of redox potentials with such large [ADP][P_i]/ATP values is due to a reversal of electron transfer accompanied by an accumulation of the inhibited high-energy forms of the respiratory carriers. The latter reaction apparently proceeds to such an extent that the interaction of the components of the chain as a whole is sufficiently slow to enable the rapid interaction with adenosine triphosphate to control the redox-level of various couples in the chain. Thus the present work emphasizes the formation of inhibitory compounds on addition of adenosine triphosphate, whereas previous work emphasized the reversal of inhibition on adding adenosine diphosphate and inorganic phosphate[25].

Relation to Adenosine Triphosphatase Activity

In considering a difference between the 'conservative' breakdown of adenosine triphosphate in a reaction yielding oxidation of cytochrome, and reduction of pyridine nucleotide and a 'dissipative' breakdown of adenosine triphosphate without such conservation of energy, it is useful to consider the sequence of equations:

$$\mathrm{ATP} + X \leftrightarrow \mathrm{ADP} + X \sim \mathrm{P} \quad (2)$$

$$X \sim \mathrm{P} + \mathrm{I} \leftrightarrow X \sim \mathrm{I} + \mathrm{P_i} \quad (3)$$

$$X \sim \mathrm{I} \overset{DNP}{\leftrightarrow} X + \mathrm{I} \quad (4)$$

Reaction 4 would correspond to 'dissipative' reaction and reaction 5 to a 'conservative' reaction:

$$X \sim \mathrm{I} + rfp + \mathrm{DPN} \leftrightarrow \mathrm{DPNH} + fp + X + \mathrm{I} + \mathrm{H^+} \quad (5)$$

Cross-over Points for Adenosine Triphosphate Interaction

Reaction 5 is based on the evidence of Fig. 6, namely, that flavin oxidation and pyridine nucleotide reduction occur in the system inhibited by quinoline-N-oxide; both the flavin and the pyridine nucleotide are associated with the side pathway involved in succinate-linked reduction of pyridine nucleotide[2,25,27]. There appears to be a cross-over point for the oxidation-reduction reaction induced by adenosine triphosphate, which corresponds to a cross-over point between reduced diphosphopyridine nucleotide and flavin observed in response to adenosine diphosphate under appropriate conditions[28]. We have not yet discovered suitable conditions for demonstrating clearly other cross-over points which would indicate further similarities in the interaction sites for adenosine tri- and di-phosphate, one being expected between cytochromes *c* and *a*, and another between cytochromes c_1 and *b* (refs. 13, 28). It is apparent from these results that the behaviour of cytochrome *b* differs sharply from that of cytochrome *c*, the latter being rapidly oxidized and cytochrome *b* being slowly reduced. Thus a second cross-over point exists in this region of the chain. It remains to determine the role of cytochrome c_1 in this transition by work on 'trapped' steady states at liquid-nitrogen temperatures.

So far, no indication has been obtained of a cross-over point between cytochrome *c* and *a*, although this, of course, does not signify that the interaction does not occur here[28]. Thus there is no evidence available at the present time which indicates that the sites at which adenosine triphosphate interacts with the respiratory carriers to give 'reversed' electron transfer differ from the sites at which adenosine diphosphate is phosphorylated to adenosine triphosphate by means of 'forward' electron transfer.

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Note added in proof. In work "On the Reversibility of Oxidative Phosphorylation", an oxidation of cytochrome *c* and reduction of flavoprotein induced by adenosine triphosphate have been observed in aerobic suspensions of rat skeletal muscle mitochondria[29]. More recently, it has been suggested that the aerobic results indicate an inhibition of electron transfer and not its reversal[30].

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SUBMOLECULAR STRUCTURE OF THE NUCLEIC ACIDS

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THE determination of the molecular structure of nucleic acids, which reveals the nature and mutual arrangement of the molecular species forming the giant polymers, is one of the most important achievements of modern biochemistry. The next logical step is the determination of the sub-molecular structure of these acids, which reveals the electronic structure of the constituents and the nature of the bonds which unite them. The establishment of the principal features of this sub-molecular structure should provide the proper basis for the understanding of the essential chemical, physico-chemical and biochemical properties of the nucleic acids.

Among the methods available for this investigation are the theoretical procedures of quantum chemistry, such as the valence bond or the molecular orbital

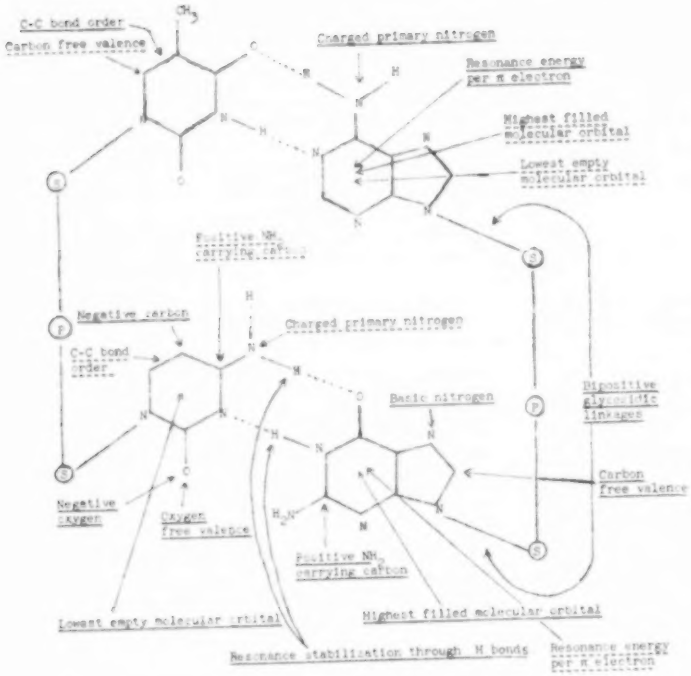

Fig. 1. Outstanding electronic indexes of the nitrogenous bases of nucleic acids

methods. This last method, in particular, has been shown in recent years to be of great value for the study of the electronic structure of biochemicals and of the mechanism, at the electronic level, of biochemical processes. It has been applied extensively, in our laboratory, to the detailed investigation of the electronic aspects of the structure of the nucleic acids and especially of that of their purine and pyrimidine bases.

This work enables the determination of the values of the essential energetic and electronic indexes characteristic of the bases or of their constituent atoms or groups of atoms. It thus also renders possible the determination of the sites at which any particular index has its most significant value. Consequently, it enables the establishment of correlations between these outstanding values of the indexes and the essential chemical and physico-chemical properties of the nucleic acids.

The principal results obtained are summarized in Table 1.

A more pictorial representation of these general results is given in Figs. 1 and 2. They contain the fundamental base pairs as present in the nucleic acids (*S* = sugar, *P* = phosphate). Fig. 1 indicates the sites at which the essential theoretical indexes of electronic structure possess their most significant values. In fact, the indexes are underlined by a heavy line when placed at the site of their most significant value and by a broken line at their next most important site.

In Fig. 2, the same thing has been done for the different chemical or physico-chemical properties determined by these indexes. In some cases, indexes or properties have been indicated on Figs. 1 and 2 without being underlined. This signifies that these indexes or properties are important characteristics of the corresponding bases, but that it is not possible to ascertain and compare their relative values in the different units.

The advantage of the schematic representation given in Figs. 1 and 2 is that it enables a very quick localization of the principal reactive centres of nucleic acids towards given types of reagents.

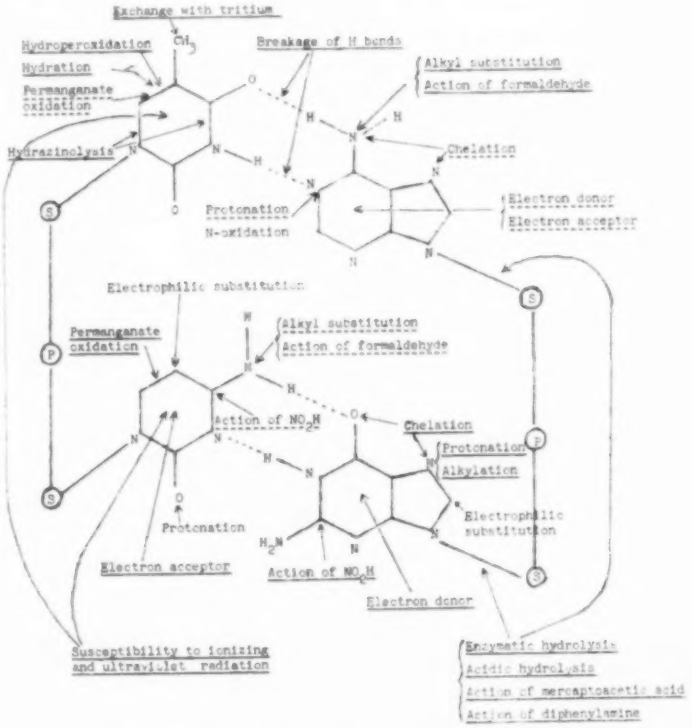

Fig. 2. Principal chemical and physico-chemical properties of the nitrogenous bases of the nucleic acids

Table 1. Fundamental Electronic Indexes and Outstanding Chemical and Physico-Chemical Properties of the Nucleic Acids

The electronic index	Its manifestation
Resonance energy. The greatest resonance energy per π electron is that of the adenine ring. The next one is that of guanine. Resonance stabilization through hydrogen bonds is greater for the guanine-cytosine pair than for the adenine-thymine pair[1-3].	Resistance of purines and in particular of adenine to ionizing and ultra-violet radiations[7]. Higher temperature of denaturation of nucleic acids rich in guanine-cytosine pair, than of those rich in adenine-thymine pair[8].
Highest filled molecular orbital. The highest filled molecular orbital is the highest in guanine followed by adenine[4,5].	The electron donor properties of purines, visible in their tendency to form charge-transfer complexes with different electron acceptors[4,6].
Lowest empty molecular orbital. The lowest empty molecular orbital is the lowest in cytosine, followed by adenine[4,5].	The electron acceptor properties of these two bases, visible in their tendency to trap electrons[5].
Basicity of ring nitrogens. In the nucleic acids the most basic nitrogen is predicted to be N_3 of guanine. In adenine the essential basic centre should be N_1 (in nucleic acid adenine it may be N_7)[1,2].	Protonation and alkylation by alkylating agents occur at N_7 of guanine and N_1 of adenine[7-9]. N-oxidation occurs at N_1 of adenine[10]. Alkylation of nucleic acids by alkylating agents occurs essentially at N_7 of guanine[11-13]. The principal site of chelation by metals is between N_7 and the O of guanine[14].
	Direct alkyl substitution at the amino-group and the reaction with formaldehyde occur essentially on the NH_2 groups of adenine, followed by that of cytosine[15-17].
Charge of the primary amino-nitrogen. Because of the delocalization of their lone pairs the nitrogens of the NH_2 groups are formally positive. The most charged among them (the less positive) is that of adenine, followed by that of cytosine[1].	Deamination of deoxyribonucleic acid by NO_2H occurs essentially on guanine, followed by cytosine[18].
Charge of the carbon atoms carrying the amino-groups. These carbon atoms are formally positive. The most positive among them is that of guanine, followed by that of cytosine.	The oxygen of cytosine may be the primary site of protonation of undenatured deoxyribonucleic acid[19].
Charge of the oxygen atoms. The most negative oxygen is that of cytosine[1].	Hydroperoxidation under the action of ionizing radiations and hydration upon photolysis occur essentially at the C_5–C_6 bond of thymine[3]. Permanganate oxidation occurs essentially at the C_5–C_6 bond of cytosine, followed by that of thymine[20].
Carbon-carbon bond order. The greatest C-C bond order is that of the 5-6 bond of thymine, followed by the 5-6 bond of cytosine[3].	Both carbons are sites of electrophilic substitutions[21].
Indexes of unsubstituted C atoms. C_8 of guanine has the greatest free valence, C_5 of cytosine the greatest formal negative charge[1,2].	Preferential reactivity of the glycosidic linkages of the purines in enzymic or acidic hydrolysis[22] and towards mercaptoacetic acid and diphenylamine[23,24].
Bipositivity of the C-N glycosidic linkage. The formal positive charge of the sugar carrying nitrogen and the bipositivity of the glycosidic linkage are greater for the purines than for the pyrimidines[22].	

In this respect, one of the striking features of Fig. 2 is that none of the quoted reactions appears heavily underlined for the adenine ring. (It is only the transformations which are concerned with its extracyclic NH_2 group which appear as occurring with particular ease at that molecule.) The relatively great stability of adenine towards external agents of any type is thus immediately visible after a simple glance at Fig. 2. This impression is still substantiated by a glance at Fig. 1 on which the only characteristic of the adenine ring which deserves the heavy underlining is its relatively great resonance energy. The particular part played by adenine in biochemistry has been tentatively linked with its particularly pronounced thermodynamic and kinetic stability[2].

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DETECTION OF LIVER PROTEINS IN CIRCULATING BLOOD

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THE release of proteins from rat liver during perfusion of this organ with rat blood[1] can be demonstrated by means of rabbit antiserum against a homogenate of whole rat liver using the gel precipitation method of Ouchterlony[2]. To avoid precipitation lines due to the rat plasma proteins, the antiserum was always adsorbed with rat plasma before use. When the antiserum was allowed to react with the liver homogenate against which it was formed, 8–10 lines were obtained. Under similar conditions, plasmas from blood which had been used for perfusion of a rat liver for 4–5 hr. gave 2–6 lines. As may be seen in Fig. 1, both the number and the intensity of the lines produced by plasmas from different liver perfusions varied very greatly. The experiment (Fig. 1) also shows immuno-

logical identity, or partial identity, between proteins of the liver homogenate and those liberated during perfusion of the rat liver.

Altogether, plasmas from thirteen perfusion experiments were examined by means of the antiserum. In eight of these, heparin was present as the anticoagulant. In three the freshly drawn blood was mixed with 0·167 vol. of 3·8 per cent sodium citrate. After centrifugation the plasma was clotted by the addition of calcium ions. The serum thus obtained was then re-mixed with the red cells. In the last two experiments no sodium citrate was used, the blood being centrifuged in plastic tubes, separated and the plasma allowed to clot. After removal of the fibrin the serum was re-mixed with the red cells. In the last five experiments the only fibrinogen or fibrin which can have been present will have been that formed by the liver during the course of the perfusion.

When heparin was used the precipitation lines formed by the antiserum as judged by eye, although very variable in intensity, were on average much heavier than those which were formed after addition of citrate and removal of fibrin. The two plasmas which appeared to contain the smallest amounts of solubilized liver protein were from experiments of the latter kind. On the other hand, in another experiment of this kind, heavier precipitation lines were observed. Both the plasmas which had been defibrinated and then used without added sodium citrate gave rather heavy precipitation lines with the antiserum. In one of these experiments the perfusion-rate fell progressively and, at the end, material which seemed to be fibrin was found adhering to the glassware. Although experimental conditions for the perfusion of rat livers which will completely prevent the solubilization of even small amounts of liver material have not yet been completely defined, the above results with defibrinated blood containing citrate suggest the usefulness of such media.

Because of the apparent readiness with which certain components appeared in the plasma during perfusion of the isolated liver, conditions which would lead to release of proteins from the liver *in vivo* were sought. Plasmas were examined from rats subjected to: (1) Repeated injection with large amounts of indian ink over four days (for details, see Freeman, Gordon and Humphrey[3]). (2) Anaphylaxis; a rat previously sensitized by means of haemocyanin in Freund's adjuvant was injected intravenously with 2 mgm. of alum precipitated haemocyanin. Two hours after the commencement of severe, but non-fatal anaphylaxis, the animal was bled. (3) Intravenous injection of the lipopolysaccharide endotoxin of *E. coli* 08 (from Prof. O. Westphal). Whereas no effect could be detected as a result of either of the first two treatments, plasma obtained 6 hr. after the injection of 1 mgm. of the endotoxin already yielded a single precipitation line. After a further 16 hr. the plasma from the same animal gave three lines. The rat which showed minimal signs of prostration was then killed. The liver showed many pale spots.

The identity or otherwise of the liver components released into the plasma *in vivo* by the endotoxin with those appearing after perfusion of a liver for several hours was also examined. In all experiments continuity of the precipitation lines formed between the antiserum and plasmas from each kind of experiment was observed. Apparently no components present in one plasma were completely absent from the other. On the other hand, large quantitative differences between certain components were noticeable.

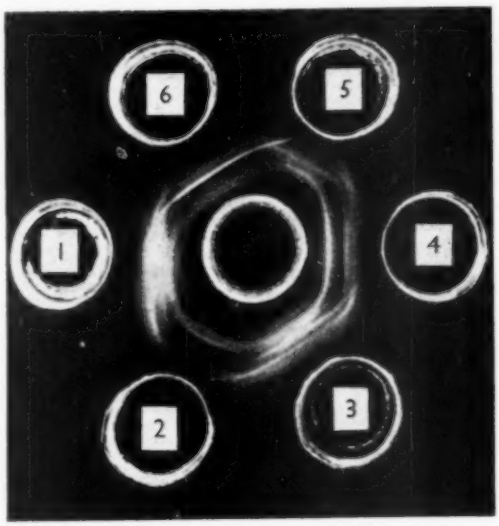

Fig. 1. Centre hole: antiserum produced in rabbits by injection of rat liver homogenate treated with Freund's adjuvant. The antiserum has been absorbed by subsequent addition of rat plasma. (1) and (3) Rat liver homogenate diluted with 9 vol. of saline; (5) rat liver homogenate diluted with 19 vol. of saline; (2) plasma from rat blood used for perfusion of a rat liver for 4 hr.; (4) plasma from rat blood used for perfusion of a rat liver for 5 hr.; (6) plasma from rat blood used for perfusion of a rat liver. For this perfusion the plasma protein concentration was raised to 104 mgm. per ml. Heparin was used in each of these perfusion experiments

In order to obtain information on the amount of material passing from the liver into the circulating blood during a perfusion experiment, comparison was made between the precipitation lines given with the antiserum by appropriate dilutions of a saline extract of rat liver and by samples of plasma from blood after use for perfusion. Appropriate dilutions of the liver extract and dilutions of the perfusion plasma were arranged alternately around a central well. By observing which samples gave precipitation lines of similar intensity and position, it was possible to estimate the dilution of liver extract containing amounts of particular liver components corresponding to those in the perfusion plasma.

Three samples of plasma taken at the end of three liver perfusion experiments were thus investigated. The first was from a perfusion in which heparin was present and in which the plasma protein concentration had been increased above normal. This plasma was found to contain at least 3·5 mgm. per ml. of liver protein. The two other plasmas, from experiments in which defibrinated blood containing sodium citrate had been used, gave 0·23 and 2·1 mgm. per ml., respectively. Considered in relation to the total weight of protein in the perfused liver, these figures indicate that at least 0·5–5 per cent of originally intracellular material had appeared in the circulating plasma.

I am very grateful to Dr. J. H. Humphrey for advice on the immunological methods used in the present work and for discussion of the problem.

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AFFINITY OF ORGANIC COMPOUNDS FOR FREE ELECTRONS WITH THERMAL ENERGY: ITS POSSIBLE SIGNIFICANCE IN BIOLOGY

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MANY molecular species react with free electrons to form stable negative ions. In the classical physical researches on the behaviour of free electrons in gases[1–3], the study of negative-ion formation was restricted to a few simple substances such as water, oxygen and the halogens. More recently, a technique has been developed for observing the electron affinity of volatile organic substances generally[4]; this technique was primarily intended as a qualitative analytical method for the identification of minute quantities of volatile organic compounds. It was based on the observation that the electron affinity of a homologous series of compounds was determined principally by the affinity of the common functional group and was relatively independent of the hydrocarbon moiety. The establishment of this method requires measurement of the electron affinities of a wide range of compounds at various electron energies; this is a lengthy task and not yet completed. In the course of this investigation it has been observed that the affinities of compounds for electrons with thermal energies are frequently associated with their biological activity, particularly in those systems thought to involve electron transport. For example, among the few simple aliphatic compounds with an extreme affinity for electrons are the intermediates on the oxidation pathways of the living cell, such as pyruvate and fumarate. The potential interest of this and other similar comparisons between biological activity and electron affinity encouraged the preliminary report which follows. It describes briefly the methods used to measure the affinities of organic substances for thermal electrons and includes a discussion of the general problem of electron transport in the living cell in the light of these new measurements.

Physical basis and experimental method. Free electrons and molecules react to form stable negative ions by either of the two following processes:

$$e^- + AB = (AB)^- + \text{energy} \qquad (1)$$

$$e^- + AB = A + B^- \pm \text{energy} \qquad (2)$$

In the first reaction, the energy released may escape as radiation or be shared with other molecules during subsequent collisions. The energy balance of the second reaction is determined principally by the following factors: the relative kinetic energies of the reactants before and after collision, the energy released by the formation of a negative ion from a constituent atom or radical of the compound and the energy released or required to dissociate the molecule. Whichever of these reactions takes place, electrons are lost and stable negative ions formed. The probability of electron capture by a given compound depends on the elementary composition and structure of its molecules and on the kinetic energy of the colliding electrons. In the analytical application, it is convenient to observe the spectrum of affinity of a given molecular species at different electron energies. In the present work the affinities of different substances were observed using electrons in thermal equilibrium with gas mixtures at temperatures of 20°–200° C. This range of energies is presumably similar to that of free electrons, should they so exist, in biological systems.

The apparatus used is illustrated as a schematic diagram (Fig. 1). It consisted of a plane parallel ionization chamber with an electrode separation of 1 cm., and was identical in construction to that described for another purpose[5]. The chamber was swept continuously by a stream of clean dry argon containing 0·3 per cent of hydrogen at a rate of 100–1,000 ml. per min. at atmospheric pressure. Electrons were set free in the chamber by means of soft β-radiation from a sheet of metal coated with a thin layer of titanium tritide; this radiation source also served as the cathode of the chamber. The density of free electrons in the chamber was measured by applying to the anode, every 10 μsec., a rectangular pulse 50 V. in amplitude and 0·5 μsec. in duration. The duration of this sampling pulse was chosen to be just sufficient to collect all the electrons set free in the chamber; in other words, capable of withdrawing a saturation current from the chamber. Such a pulse duration was, however, much too short to collect any of the relatively immobile negative molecular ions. The contribution to the total current-flow of electrons liberated during the application of the pulse was only 5 per cent; the loss of electrons, when vapours capable of capturing them were present in the chamber, was therefore observed effectively under field-free conditions and when the energy of the electrons present was thermal. The vapours of the test substances were introduced into the gas stream flowing to the chamber after their passage through an efficient 100-ft. capillary tube chromatograph column. This precaution was found essential since few of the substances tested were free of electron-capturing contaminants. The concentration of vapour in the gas stream was measured by means of a photo-ionization detector[6] connected in parallel with the chamber for observing electron capture. The current-flow from the two ionization chambers was amplified by electrometer amplifiers and recorded using two separate potentiometric recorders.

Fig. 2 illustrates a typical measurement in which the emergence of several compounds in sequence from the chromatograph column is displayed as chromato-

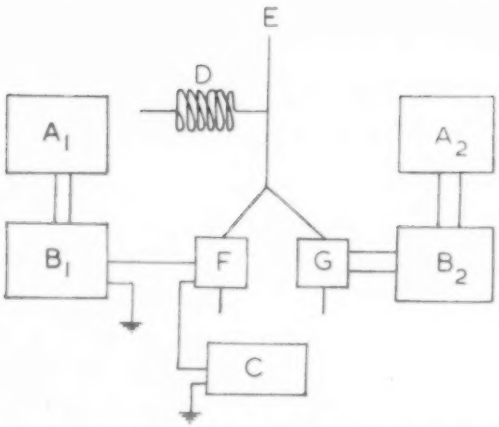

Fig. 1. Schematic diagram of the apparatus used for the measurement of relative electron affinities. A_1 and A_2 potentiometric recorders, B_1 and B_2 electrometer amplifiers, *C* a pulse generator, *D* a capillary tube chromatograph column, *E* inlet for diluent gas, *F* the ionization chamber for observing electron capture and *G* a photo-ionization detector for the measurement of concentration of test vapour

grams. The lower chromatogram shows the vapour concentrations of the test substances and the upper shows the extent of electron capture. The small vapour concentrations of the test substances, ethyl pyruvate and dimethyl fumarate, are seen to capture electrons much more readily than the large vapour concentration of the reference substance, chlorobenzene. Also, the test substance, diethyl succinate, is seen to have little or no affinity for electrons. The relative electron affinities of the different substances tested were compared in terms of the ratio of the change of current in the two ionization chambers and are expressed always as relative to the reference standard, chlorobenzene. Whenever possible, the quantity of test substance used was adjusted so that the change in current in the electron-capture chamber did not exceed 10 per cent of the total current. Above this value the change of current is no longer linearly related to vapour concentration. To meet this need, quantities of between 10^{-6} and 10^{-9} gm. were applied to the column. It must be emphasized that the electron affinities reported here may be as much as 30 per cent in error. Uncertainties arise principally in the measurement of vapour concentration. It is not yet possible to apply precisely known amounts of test substances to the efficient capillary tube column. Also, the response of the photo-ionization detector used to measure vapour concentration is not yet known with precision. This detector was chosen for this application because it is the only available sensitive ionization detector the response of which is not adversely affected by substances with a high affinity for free electrons.

Relative electron affinities of the substances tested. Table 1 lists the electron affinities, relative to chlorobenzene as unity, of the strongly electron-attracting substances tested; also shown are the principal electron-attracting substituents or structures of these substances and the electron affinities of comparable weakly attracting compounds.

The great majority of simple aliphatic organic compounds possess a slight or negligible affinity for free electrons of thermal energy. Those which do capture electrons strongly have one or more of the following structures or substituents in their molecules, which henceforth will be called 'electrophores': (1) —CO.CO—, (2) —CO.CH : CH.CO—, (3) the quinone structure, (4) $—NO_2$, (5) —*X*, where *X* is one or more halogen atoms. With substitution by halogens affinities fall in the order: I > Br > Cl > F; multiple substitution by halogen- or nitro-groups greatly enhances the affinity for electrons.

It is probable that other more or less complex structures can function as electrophores. Thus, although simple conjugated and aromatic hydrocarbons such as butadiene, benzene, naphthalene and phenanthrene show little affinity, more complex conjugated hydrocarbons, including *cyclo*-octatetrene, azulene, diphenyl butadiene and anthracene, all show a marked affinity for free electrons. It appears also that [—CO.] in the electrophores listed above can be replaced by a phenyl radical without great loss of affinity; a substitution of nitrogen in place of carbon can also be made. It must be emphasized, however, that affinity of a high order, greater than ten, is rare among the simpler organic compounds. An affinity of this order has not been found during the examination of 430 members of the following classes of organic compounds: saturated, ethenoid and ethinoid hydrocarbons, ethers, esters, alcohols, carboxylic acids, aldehydes, ketones, nitriles, amines and, with the exceptions listed in Table 1, compounds with two or more of these groups. Although weakly attractive to thermal electrons, the compounds just listed do possess a sufficient affinity for analytical purposes.

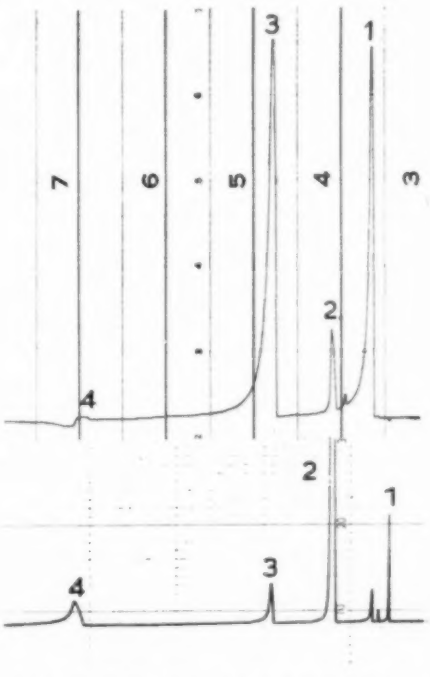

Fig. 2. Measurement of electron affinity using the apparatus indicated in Fig. 1. The lower chromatogram shows the concentrations of vapours emerging from the chromatograph column, the upper chromatogram the capture of electrons by the same vapours measured simultaneously. The test substances are: ethyl pyruvate (1), chlorobenzene (2), dimethyl fumarate (3) and diethyl succinate (4)

Table 1. AFFINITIES FOR THERMAL ELECTRONS OF COMPOUNDS OF BIOLOGICAL INTEREST

All values are relative to the electron affinity of chlorobenzene, which is taken to be unity

Compounds with high electron affinity	Electrophore	Affinity	Compounds with low electron affinity	Affinity
Ethyl pyruvate	—CO.CO—	1,700	Ethyl acetate	< 0·01
Diacetyl	—CO.CO—	2,000	Acetylacetone	1·2
Dimethyl oxalacetate	—CO.CO—	1,300	Ethyl acetoacetate	0·7
Diethyl fumarate	—CO.CH : CH.CO—	1,500	Ethyl acrylate	0·1
Diethyl maleate	—CO.CH : CH.CO—	1,700	Diethyl malate	0·01
			Diethyl succinate	< 0·01
Quinone	*Q*	5,000		
Dimethylnaphthaquinone	*Q*	4,100	Hydroquinone	0·1
Benzaldehyde	—CO.*P*	48	Benzyl alcohol	0·05
Cinnamaldehyde	—CO.CH : CH.*P*	310		
cis-Stilbene	*P*.CH : CH.*P*	1	Styrene	< 0·01
trans-Stilbene	*P*.CH : CH.*P*	4		
Acetamide	—CO.NH$_2$	12	Methyl amine	0·01
Azobenzene	*P*.N : N.*P*	9	Aniline	0·1
Diacetyldihydropyridine	*Q*	4,000	Pyridine	0·02
Anthracene		12	Phenanthrene	0·05
Azulene		340	Naphthalene	< 0·01
Cyclo-octatetrene		210	Cyclopentadiene	< 0·01
Carbon tetrachloride	—Cl	7,000	Ethane	< 0·01
Chloroform	—Cl	800		
Hexachlorobenzene	—Cl	1,100	Benzene	< 0·01
Chlorobenzene	—Cl	1		
Bromobenzene	—Br	6		
Iodobenzene	—I	370		
Nitrobenzene	—NO$_2$	390		
Dinitrophenol	—NO$_2$	1,450		

P, phenyl radical. *Q*, quinone structure.

At present no information is available concerning the end products of the reaction between the compounds tested and free electrons. It is probable, however, that capture is followed by dissociation with the halogen- and nitro-compounds. The hydrocarbons and perhaps some CHO compounds are, on the other hand, likely to form stable negative molecular ions.

Relevance to biological systems. It has been suggested that protein may show semi-conducting properties important in its normal function[7]. More recently, evidence has become available to suggest that in photosynthesis[8,9] and in the transfer of energy in mitochondria[10,11], free electrons play an important part. In the light of these suggestions it is of interest that the electrophores, —CO.CO—, —CO.CH : CH.CO— and the quinone structure are all closely associated with those systems thought to be important in electron transfer. Thus, in the process of oxidative phosphorylation proceeding from pyruvate through the Krebs cycle to carbon dioxide each alternate intermediate has one or other of the two electrophores, —CO.CO— and —CO.CH : CH.CO—. The first is found in pyruvate, oxalacetate, and ketoglutarate; the second in *cis*-aconitate and in fumarate. The remaining intermediates are found in the form of their esters, or would be thought to have but little affinity for free electrons. The 'inert' intermediates, including succinate, malate, acetate, citrate and *iso*citrate, are always interposed between the electron-attracting intermediates. Two other substances thought to be important in the transport of electrons in the living cell are coenzyme *Q* and diphosphopyridine nucleotide (DPN). The former has the quinone electrophore; it is conceivable that the structure of DPN includes an electrophore as yet unidentified.

The presence in the electron transport system of the living cell of an ordered distribution of so many of the few simple organic substances likely to have a high affinity for free electrons seems to be more than coincidental. It is also remarkable that among the few remaining substances with a similar high affinity for free electrons are several which are able to disturb the process of oxidative phosphorylation, such as dinitrophenol and certain halogen-containing compounds. The significance of the association between electron affinity and biological function depends on the assumption that the electrophores are as active in the relevant compounds in their natural state as they are in the volatile esters tested. If this assumption is justified, then the observations suggest the following unifying hypothesis: electron transport in the living cell proceeds through an ordered sequence of reversible electron traps. The introduction of foreign, especially irreversible, trapping agents is harmful because of their ability to remove electrons from the normal sequence. The term reversible trap refers to a compound which after capturing an electron changes either physically or chemically to a second compound the affinity of which is slight, and so releases the electron for the next trap in the sequence. To illustrate this point, fumarate could be considered to capture an electron and the negative fumarate ion then reacts with water to form a malate negative ion; the weak affinity of malate for electrons would encourage their transfer to the next trap in the sequence, possibly DPN.

The hypothesis that electron trapping in the living cell is a purposeful process offers explanations for a number of apparently intractable problems in biological electron transport. A few of these problems, particularly those concerned with the mechanism of action of toxic substances able to disturb the normal process of electron transport, are briefly discussed as follows:

In descriptions of the mechanism of photosynthesis, it has repeatedly been stressed that some process is required to explain the rapid removal of primary electrons before they can recombine with the positive charges simultaneously produced by photon impact[12]. The trapping mechanism just described would meet this need.

The volatility of the thyroid hormones is too low to measure their electron affinity by the methods just described. It is tolerably certain, however, that these compounds, which contain three or more iodine atoms, are potent electron traps. The possibility

that the thyroid hormones owe their ability to moderate the process of oxidative metabolism to their high affinity for free electrons is supported by the following circumstantial evidence: the biological activities of trichloro-, tribromo- and tri-iodo-thyronine[13] are respectively: 1, 37 and 420. The electron affinities of chloro, bromo- and iodo-benzene are respectively: 1, 6, 370. Although the structures of the thyronines are very different from those of the halogen-substituted benzenes, the comparison is justified by the fact that the electron affinity conferred by halogen substitution is frequently independent of the nature of the molecule substituted; provided, of course, no other electrophores are also present. The resemblance between the biological activity of the thyroid hormones and that of dinitrophenol is further evidence in support of this interpretation.

Another reaction in biochemistry thought for some time to involve electron transfer is that between carcinogenic hydrocarbons and protein. A stumbling block to the understanding of the nature of this reaction has been the persistently held assumption that the hydrocarbon is the donor and the protein the acceptor of electrons; this has been difficult to reconcile with theory or observation. It was suggested tentatively[14,15] that these difficulties could be resolved if the hydrocarbon were in fact the acceptor of electrons. The unpopularity of the notion of a hydrocarbon so behaving in that way seems to have prevented the general acceptance of the suggestion. However, as shown in Table 1, complex hydrocarbons are very ready to function as electron acceptors. Because of their slight volatility, it has not yet been possible to test the carcinogenic hydrocarbons themselves, although it is of interest that stilbene and azobenzene both are able to capture electrons and give rise to simple derivatives with carcinogenic activity.

In general, where a similar toxic action is shared by compounds differing only in substitution with halogen- or nitro-groups, and where a disturbance of electron transport is thought to occur, then the toxicity of the compounds could be due to their ability to trap electrons. One important difference between normal intermediates which can trap electrons and the toxic substances could be in the type of reaction which takes place. Trapping of electrons is potentially most harmful when it is irreversible; in these circumstances, the potential energy of the captured electron may be completely removed from the system. Furthermore, if dissociative capture occurs, and it is likely to occur with halogen- and nitro-compounds, then a highly reactive and potentially harmful free-radical may be formed. In addition to those classes of toxic agent already mentioned, other substances which may function in a similar way include halogenated insecticides, inhibitors of plant growth, certain fungistatic iodo- and nitro-compounds[16] and certain antibiotics such as chloramphenicol. Some of the limitations of the evidence provided from measurements of electron affinity arise from the need to conduct the observations on volatile derivatives in the gas phase. There is no reason in principle why similar measurements to those described should not be made in the liquid or even solid phases. The solution of the practical problems in this direction will greatly extend the range of measurement of this potentially important molecular property, and perhaps provide the evidence necessary for the confirmation or denial of the hypotheses outlined in this article.

I am indebted to my colleagues T. Nash and N. L. Gregory for the stimulus of their suggestions.

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AGGREGATION, VARIANCE AND THE MEAN

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IN populations where the individuals are distributed at random, that is, are independent of each other, the variance (s^2) at each population density is equal to the mean (m). Individuals in natural populations are not, however, independent of each other; mutual attraction leads to aggregation which makes variance more than the mean ($s^2 > m$), and mutual repulsion leads to regularity which makes variance less than the mean. Hence, in Nature, true randomness is only one of a continuous series of possible distributions (both in a spatial and a statistical sense) from regular to highly aggregated, and is consequently rare.

This property of natural populations, to show some degree of aggregation, is commonly thought to be highly specific; for example, soil zoologists know that leather-jackets are 'more highly aggregated' than wireworms, yet the meaning of this is intangible, because no consistent measure of aggregation is at present available. In addition, many kinds of statistical analysis require that the variance should be made independent of the mean and there is no rational transformation available covering all grades of aggregation. Aggregation has been measured most widely using k in the expression:

$$s^2 = m + km^2 \qquad (1)$$

derived from the negative binomial distribution. Unfortunately k is not always independent of m (ref. 5), and it is plainly desirable that an index of population structure should be the same at different

population densities, unless some actual change in behaviour is involved.

In all the sets of samples I have examined, variance appears to be related to the mean by a simple power law; variance is proportional to a fractional power of the mean:

$$s^2 = am^b \qquad (2)$$

where a and b are characteristic of the population in question. This is most clearly demonstrated by a log – log plot of s^2 on m as in Fig. 1, which includes some classic population surveys. Table 1 gives a and b for these and other populations, namely, virus lesions, macro-zooplankton, worms and symphylids in soil, insects in soil, on plants and in the air, mites on leaves, ticks on sheep and fish in the sea.

Table 1

	Name	Site and sample	Range of m	Range of s^2	N	a	b	Transformation	Observer (refs. in brackets)
1	Shellfish on seashore, *Tellina tenuis* da Costa, Eulamellibranchiata : Mollusca	Sand, 63 units, various sizes	0·72–45·7	0·49–8·0	5	0·50	0·70	$x^{0.70}$	Holme (13)
2	European chafer larvæ, *Amphimallon majalis* Raz. (= *Melolontha melolontha* L.), Coleoptera : Insecta	Pasture soil, 25 units, each 1 ft. sq.	0·20–9·72	0·26–14·93	75	1·15	1·07	$x^{1.07}$	Burrage and Gyrisco (6)
3	Flying insects, various orders : Insecta	Open air, 16–104 units aerial density	1·9–238	1·7–606	24	1·0	1·17	$x^{1.17}$	L. R. Taylor (unpublished)
4	Wireworms, *Agriotes* spp. mainly *obscurus*, Coleoptera : Insecta	Grassland soil 20 units, 4 in. cores	0·20–4·65	0·40–17·80	2,372	2·75	1·19	$x^{1.19}$	Yates and Finney (23)
5	Wireworms, *Agriotes* as above	Arable land soil 20 units, 4 in. cores	0·20–4·65	0·39–22·50	525	2·85	1·26	$x^{1.27}$	Yates and Finney (23)
6	Wireworms, *Limonius* spp., Coleoptera : Insecta	Arable land soil, 175 units, each 1 ft. sq.	0·39–10·89	0·58–60·42	24	2·0	1·33	$x^{1.33}$	Jones (5, 14)
7	Gall midge larvæ, *Jaapiella medicaginis* (Rub.), Diptera : Insecta	Lucerne field soil, 10 units, 4 in. cores	0·22–5·6	0·19–13·82	15	1·3	1·33	$x^{1.33}$	Heath (12)
8	Spruce budworm larvæ, *Choristoneura fumifera* (Clem.), Lepidoptera : Insecta	Fir foliage, 25 units, larvæ/twig	0·48–15·04	0·343–51·86	50	1	1·40	$x^{1.40}$	Waters (4, 22)
9	Virus lesions, tobacco necrosis virus	Bean leaves, 4 units, lesions/half leaf	15·38–237·56	65·13–3,265·80	120	1	1·40	$x^{1.40}$	Kleczkowski (5, 15)
10	Colorado beetle adults, *Leptinotarsa decemlineata* Say., Coleoptera : Insecta	Potato foliage, 2,304 counts : insects/2 ft. row	1·0–12·1	1·4–37·7	16 16 5	1	1·48	$x^{1.48}$	Beall (2, 3, 5, 19)
11	Japanese beetle larvæ, *Popillia japonica* New., Coleoptera : Insecta	Soil, 10,000 units each 1 ft. sq.*	2·76–1,914	5·90–210,000	36	1·3	1·52	$x^{1.54}$	Fleming and Baker (10)
12	Macro-zooplankton	Water, net collection, slide count, 10 areas	95–1,750	1,444–194,480	4	1·0	1·57	$x^{1.57}$	Littleford, Newcombe and Shepherd (16)
13	Macro-zooplankton	As above, 50 areas	93–1,822	169–18,769	4	0·14	1·57	$x^{1.57}$	Littleford, Newcombe and Shepherd (16)
14	Ticks, *Ixodes ricinus* L., Acarina : Arachnida	Sheep, 20–86 units, ticks/sheep	0·84–85·6	2·5–2,292	10	1·0	1·66	$x^{1.67}$	Milne (18)
15	Enchytraeid worms, mainly *Fridericia bisetosa* (Lev.), Enchytraeidae : Annelida	Pasture, 60–150 units, 3·6 cm. cores	40·8–381·5	441–29,584	4	1·0	1·66	$x^{1.67}$	Nielsen (20)
16	Corn borer larvæ, *Pyrausta nubilalis* (Hubn.), Lepidoptera : Insecta	Maize stalks, 2 stage†	6·7–970	88·5–180,220	1,054	3·0	1·66	$x^{1.67}$	Meyers and Patch (17)
17	Thrips, *Thrips imaginis* (Bagnall), Thysanoptera : Insecta	Rose flowers, 20 units, thrips/rose	20·6–137·5	223–7,900	16	1·0	1·80	$x^{1.80}$	Davidson and Andrewartha (8)
18	Leather-jackets, *Tipula* spp., Diptera : Insecta	Soil, 2 units, Nos./sq. ft.	3·10–63·50	3·5–409·0	36	0·2	1·85	$x^{1.85}$	Bartlett (1, 5)
19	Earthworms, all stages, *Allolobophora chlorotica* (Sav.), Oligochaeta : Annelida	Grassland, 4 units, 18 in. sq.	2·8–71·3	2·9–1,410	54	0·2	2·00	$\log x$	Gerard (11)
20	Red spider mite, eggs and adults, *Metatetranychus ulmi* (Koch), Acarina : Arachnida	Apple leaves, 20 units, mites/leaf	8·5–216	90–55,100	162	6·4	2·19	$1/x^{1.16}$	Daum and Dewey (7)
21	Haddock, *Melanogrammus aeglefinus*, Gadidae : Pisces	Sea, 4–47 units, Nos./trawl	4·09–288	39·1–1,239,580	15	1·0	2·35	$1/x^{0.35}$	C. C. Taylor (5, 21)
22	Earthworms, all stages, *Allolobophora caliginosa* (Sav.), Oligochaeta : Annelida	Grassland, 4 units, 18 in. sq.	4·3–44·8	4·0–500	42	0·05	2·54	$1/x^{0.37}$	Gerard (11)
23	Symphyla, *Symphylella* spp., Symphyla : Myriapoda	Various soils, 60–120 units, 2½ in. cores	4·5–31·8	0·49–690	5	0·06	2·75	$1/x^{0.36}$	Edwards (9)
24	Symphyla, *Scutigerella* spp., Symphyla : Myriapoda	Various soils, 60–140 units, 2½ in. cores	1·3–31·4	0·64–1,250	6	0·035	3·08	$1/x^{0.44}$	Edwards (9)

* Units combined to cover areas varying in size from 1 sq. ft. to 100 sq. ft. † Larvæ/stalk × infested stalks/100 : this introduces some bias in the variances.

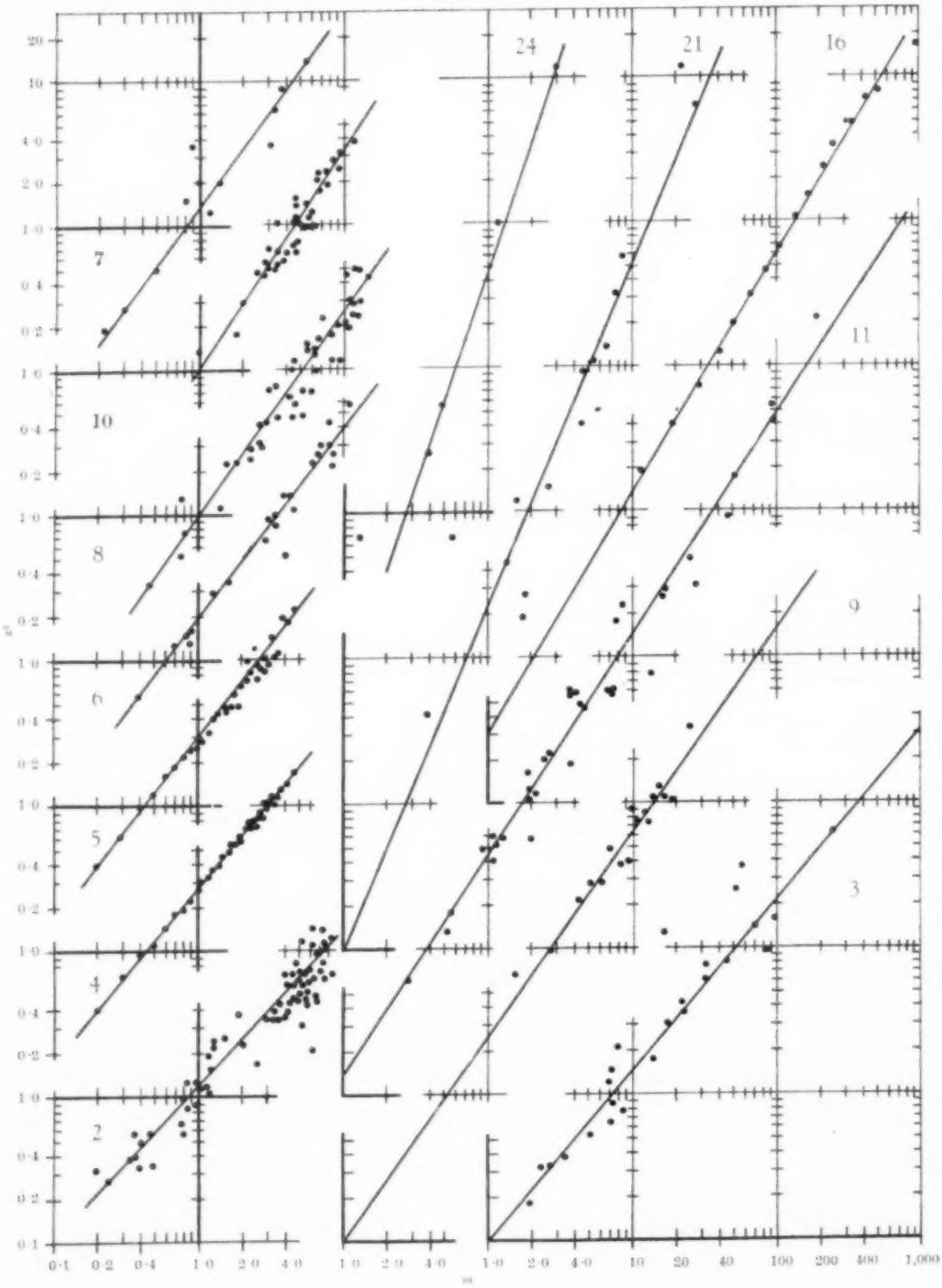

Fig. 1. Variance × mean on log × log scale for material numbered as in Table 1. The axes (heavy lines) are staggered to accommodate as much material as possible

a is evidently largely, possibly wholly, a sampling or computing factor, depending upon the size of sampling unit and on which estimate of variance is used; this was not clearly stated in some of the analyses. b appears to be a true population statistic, an 'index of aggregation' describing an intrinsic property of the organisms concerned and with a continuous graduation from near-regular ($b \to 0$), through random ($b = 1$) to highly aggregated ($b \to \infty$).

To use the analysis of variance technique raw data must first be transformed to make s^2 independent of m. Using expression (2), the general transformation:

$$f(x) = Q\int m^{-b/2}\,dm \qquad (3)$$

where Q is a constant, is obtained. Integration gives a square root transformation when $b = 1$ and, logically, a logarithmic transformation when $b = 2$, as are commonly used; for highly aggregated populations ($b > 2$) it gives a negative fractional power, for example, a reciprocal, as is appropriate to the powerful transformation required.

The power law appears to hold good down to low densities ($m < 1$) in the material examined here. This implies that populations aggregated at high density tend to become regular when density diminishes, and vice versa; the law may break down eventually or, alternatively, perhaps the concept of aggregation ($s^2 > m$) is inappropriate at these low densities. In any event samples consisting mainly of 0's and 1's are likely to need special statistical treatment.

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SURFACE ORIENTATION AND FRICTION OF GRAPHITE, GRAPHITIC CARBON AND NON-GRAPHITIC CARBON

By Dr. J. W. MIDGLEY and D. G. TEER

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THE effect, if any, of surface orientation on the friction of various carbons has not yet been clearly established. Indeed, previous reports on the orientation developed by rubbing are conflicting[1-4]. To clarify the position and hence to improve our understanding of the mechanism of the friction of wear of these materials, an attempt has been made to provide fresh evidence, notably by a comparison of the behaviour of a carbon with a very low degree of graphitization[5] with graphite and graphitic carbon. These materials have been rubbed unidirectionally and the surface orientation studied by electron diffraction.

When graphite or highly graphitic carbon is rubbed unidirectionally against itself, mild steel or paper, the surface crystallites rapidly become orientated with their (00*l*) basal planes at a small angle (5–10°) to the surface with the basal plane normals tilted against the direction of motion of the opposing surface, as shown by the electron diffraction pattern of Fig. 1. The deviation of this orientation from the parallel orientation previously reported[1-3] is small, but nevertheless significant, since, as the coefficient of friction is in the range 0·1–0·2 the present texture is consistent with a compression texture with its axis parallel to the resultant of the normal reaction and the friction forces. Similar textures have been recently reported by Porgess and Wilman[6] to be developed by graphite when abraded with emery.

The following factors could contribute to the formation of this texture: (*a*) basal plane slip; (*b*) the plate-like shape of the crystallites; (*c*) preferential removal of crystallites in other orientations.

Concerning the first of these, an electron microscope study has confirmed that, as previously reported

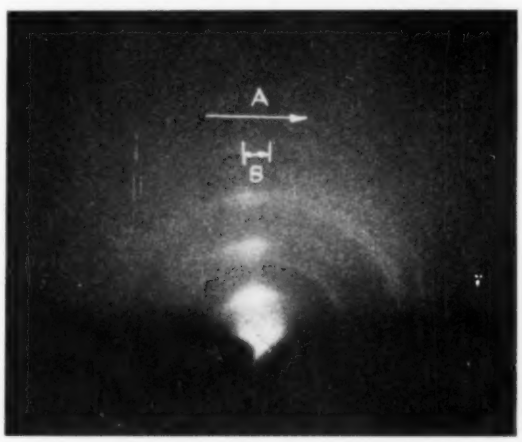

Fig. 1. Electron diffraction pattern of rubbed graphitic carbon. *A*, direction of motion of opposing surface; *B*, basal plane normals make angle of 5–10° to the surface normal

by Williamson[7] and others, basal plane dislocations are present in graphite. Furthermore, we have noted that rubbing gives rise to an extra ring in the electron diffraction patterns which coincides with the normally forbidden (111) ring and this is interpreted as arising from the presence of diffracting crystallites which have been reduced by shear to a few atom planes in the [001] direction[5]. Deacon and Goodman[3] have suggested that in the case of rubbed films of colloidal graphite the plate-like shape of the crystallites plays a decisive part in determining the surface orientation, and we believe that the shape of the crystallites will almost certainly contribute to the observed orientation on massive graphite and graphitic carbon. Finally, it is considered that the development of this preferred orientation is assisted by the preferential removal of crystallites, the basal plane normals of which are tilted in the direction of motion of the opposing surface, for such crystallites will tend to interlock and be plucked out by asperities on the opposing moving surface. The last mechanism, however, could not by itself form the observed orientation on graphite and graphitic carbon, and it is considered that with these materials the first two mechanisms are the most important.

Non-graphitic carbon behaves differently. A surface orientation does develop, but much more slowly than with graphite, and it eventually consists of crystallites the basal plane normals of which are tilted at all angles against the direction of motion of the opposing surface, as shown by the electron diffraction pattern of Fig. 2. This orientation is believed to arise from the preferential removal or wearing away of crystallites with unfavourable orientations. The structure of non-graphitic carbon does not encourage basal plane slip as there is not a unique slip direction, and the crystallite shape does not appear to play a significant part.

Simple compression tests have been employed to verify that non-graphitic carbon does not form a compression texture even when subject to a much higher compressive stress than that necessary to cause graphitic carbon to form the well-known (00*l*) compression texture. This result is in accordance with those of Bacon[9] and Ali, Fitzer and Ragoss[10], and confirms that with non-graphitic carbon the crystallite shape and slip mechanism are likely to be of minor importance in the formation of the rubbing texture.

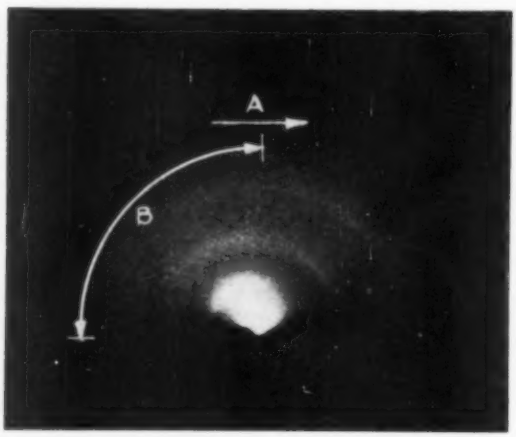

Fig. 2. Electron diffraction pattern of rubbed non-graphitic carbon. *A*, direction of motion of opposing surface; *B*, basal plane normals in this quadrant only

It has been found that the coefficient of friction of non-graphitic carbon is as low as that of graphitic carbon, and yet this low friction is achieved even though a high percentage of the surface crystallites have their basal planes at large angles to the surface. Thus, a parallel orientation is not necessary for the production of a low friction with non-graphitic carbon, and there is no reason to suppose that this is not also true for graphite and graphitic carbon. However, a temporary increase of friction of both graphitic and non-graphitic carbon has been found to occur after reversal of the rubbing direction as shown in Fig. 3 (a similar effect has been mentioned by Fullam and Savage[4]). This increase of friction is considered to arise from the interlocking of those crystallites which are in unfavourable orientations after reversal, as with fibres rubbed against the direction of the scales on their surface (cf. Bowden and Tabor[11]). The mechanism of the friction and wear of graphitic and non-graphitic carbon crystallites with unfavourable orientations is thought to be abrasion rather than intercrystallite attraction.

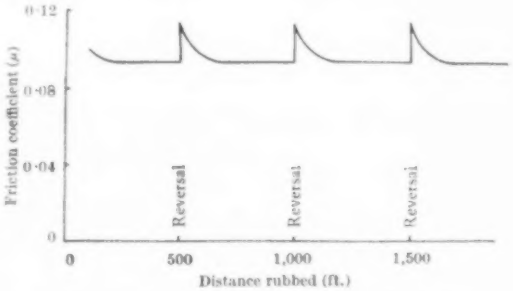

Fig. 3. Increase of friction on reversal of rubbing direction

The present results are interpreted as giving considerable evidence in support of the view that the low friction of graphite and non-graphitic carbon is due to the low adhesion between crystallites[2] rather than to low shear strength[12].

A more detailed account of this work will be published elsewhere.

We are indebted to the Directors of the English Electric Co., Ltd., for permission to publish this communication. We also wish to thank Mr. R. Brew, who took some of the electron diffraction patterns, and Mr. R. Suhr, who supplied X-ray results on the compression textures.

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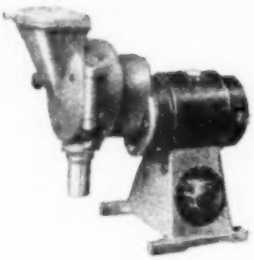

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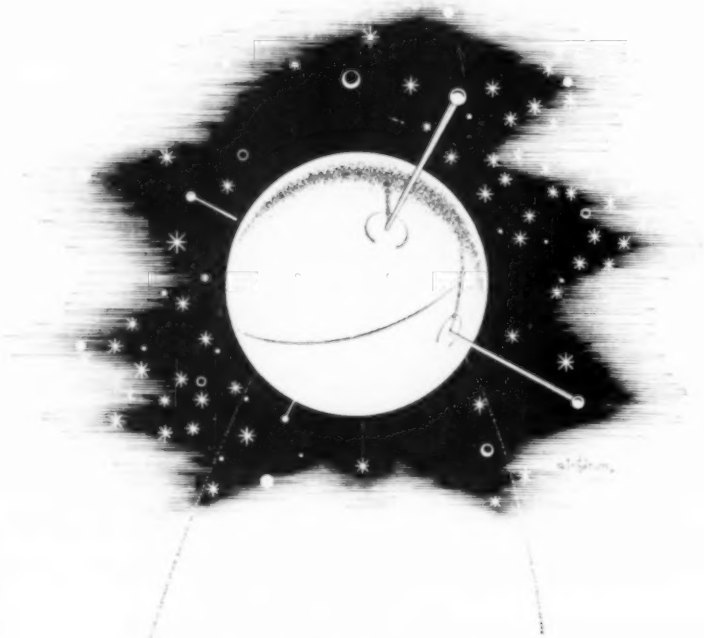

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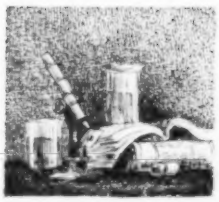

IN MARCH—(1884)—*Science* reviews a Brazilian pamphlet on the genesis of beriberi. Dr. J. B. DeLacerda cultured blood of beriberi patients in meat solution and obtained a microphyte similar to the "bacillus of carbuncle". Animals infected with this organism succumb to paralytic disease in 5 to 20 days. The microphyte was then recovered from the muscles and spinal medulla. "From these facts the author draws the logical conclusion, that beriberi is a parasitic disease, and that the parasites attack particularly the blood, muscles, and medulla."[1]

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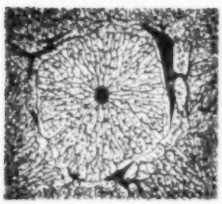

IN MARCH—(1921)—Frederick Gowland Hopkins reports the discovery of a new sulfhydryl compound in yeast, liver, and muscle cells.[2] This compound appears to contain a dipeptide of glutamic acid and cystein. Although present in low concentration, it accounts for almost all the non-protein organically bound sulfur in the cell. The cystein moiety is found to change readily from the sulfhydryl to the disulfide state under the influence of factors shown to be present in the tissues.

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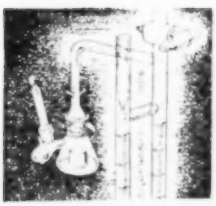

IN MARCH—(1949)—Otto Meyerhof publishes another of his interesting papers in the field of carbohydrate metabolism. Previous studies had shown that large amounts of phosphorylated hexoses are required to maintain steady continuous glycolysis in homogenates or centrifuged extracts of malignant tumors. In the absence of such phosphate donors, continuous glucose utilization can occur only if the activity of ATPase (in terms of phosphate turnover) is twice that of hexokinase. Meyerhof and Wilson[3] show that enzymatic balance may be obtained by adding yeast hexokinase or inhibiting the activity of the tumor ATPase.

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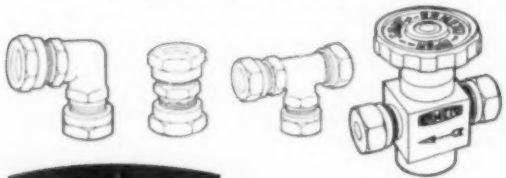

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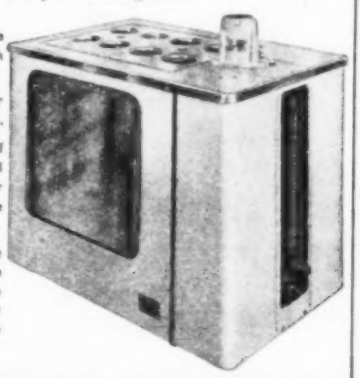

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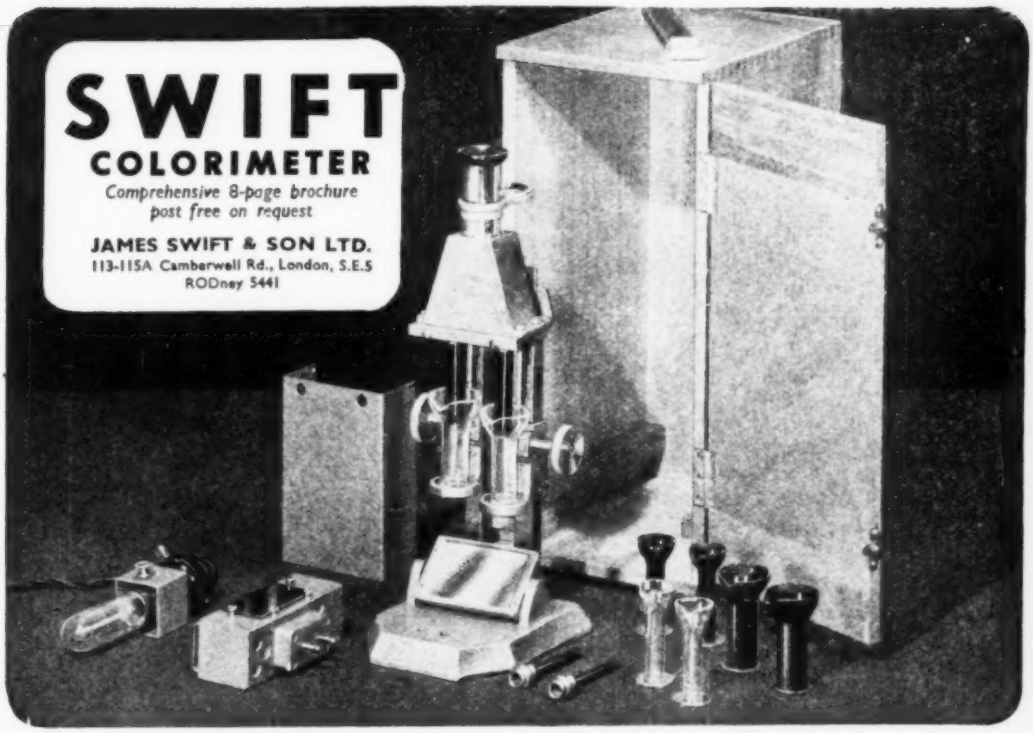

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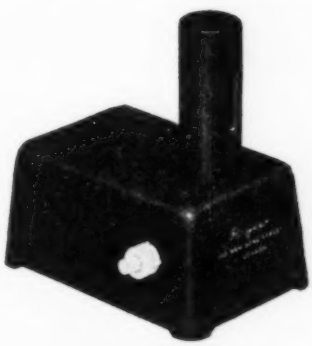

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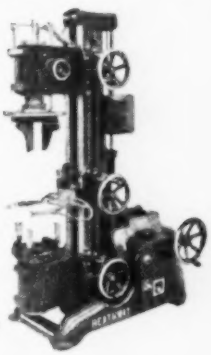

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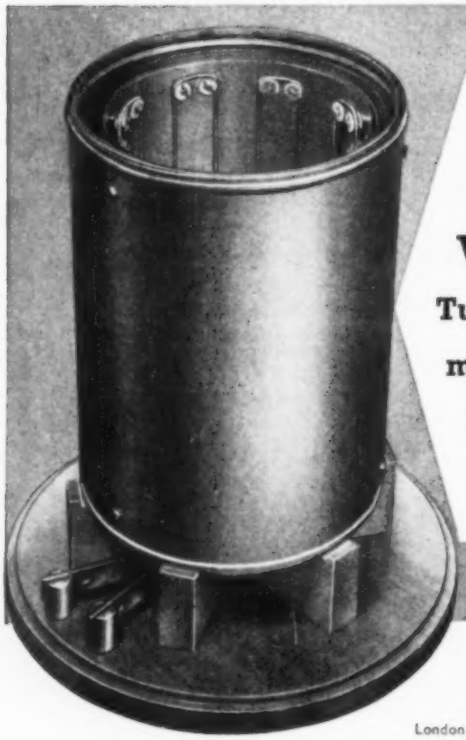

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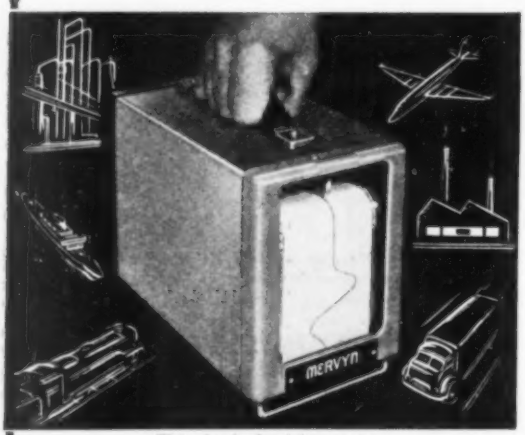

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LETTERS TO THE EDITORS

ASTROPHYSICS

Rotation Period of the Artificial Satellite 1958δ1

RECENTLY, C. R. Faulkner[1] has suggested that changes of the rotation of 1958δ1, especially the decrease of the period during the last days in November 1958, may be explained in part by a strong westerly wind in the upper atmosphere.

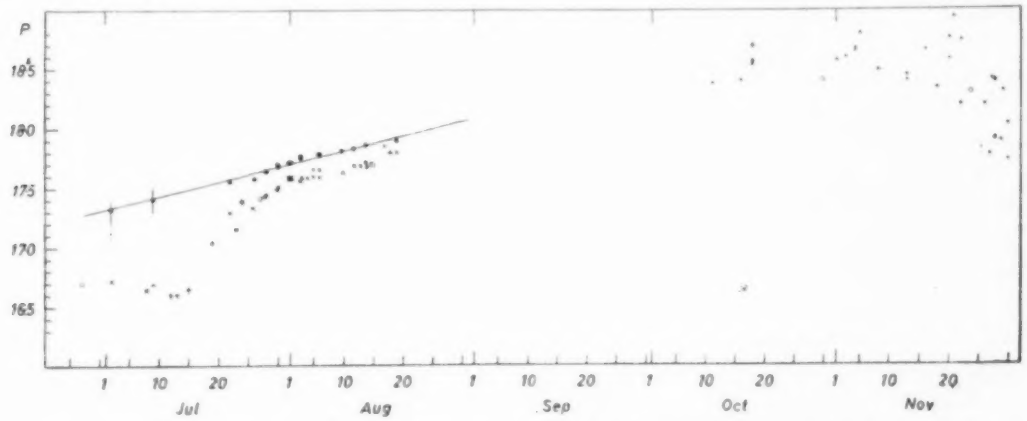

Fig. 1. Period of rotation of 1958δ1. ●, Period of rotation with limits of error (October 18: two possible solutions). ×, Period of scintillation from observations in Babelsberg and Potsdam. ○, Uncertain (November 23: amplitude of light variation very small). +, Scintillation period from some other sources (ref. 7 and Tatum, J. B., private communication)

Consider first the influence of the rotation of the Earth's atmosphere on the speed of the rotation of the satellite. According to King-Hele[2], in the presence of atmospheric rotation, a factor F, which is 0·95 for 1958δ1, must be added to the aerodynamic force acting in the direction opposite to the velocity of the satellite. Similarly, the formula for the momentum, braking the rotation of the satellite[3], must be altered to the form (neglecting for a moment the component of the atmospheric rotation acting vertically to the path of the satellite):

$$D_B = \text{const.}\,\rho B L^3 \left[v\sqrt{F}\,\omega \mathbf{F}_1 - \frac{1}{3H}\, v^2 F\, \mathbf{F}_2 \cos \angle B \right] \quad (1)$$

This formula holds for a long cylinder of diameter B and length L ($L \gg B$). $\mathbf{F}_1$ and $\mathbf{F}_2$ are the drag-coefficients for rotation; they change by a maximum of 24 per cent, depending on the position of the rotational axis. H is the scale-height of the atmosphere. $\angle B$ denotes the angle between the pole of rotation and the pole of the orbit of the satellite. The introduction of the factor F in D_B changes this momentum to approximately 0·97 (for 1958δ1) of its former value.

Further, the rotation of the satellite will be influenced by the component of the rotational velocity of the atmosphere, acting vertically to the orbit of the satellite:

$$v_\perp = r_p\, \omega_e \sqrt{(\cos^2\varphi - \cos^2 i)}$$

Here ω_e means the Earth's angular velocity, r_p is the distance from the Earth's centre at perigee, i the inclination of the orbit to the equator. This component is of influence only in the vicinity of the equator ($\varphi = 0$), but even there, its contribution is limited to a maximum of 1·5 per cent of the momentum given by (1), because its action is equivalent to a small displacement (max. ~4·) of the position of the rotational axis with respect to the orbit of the satellite. This causes the coefficients $\mathbf{F}_1$ and $\mathbf{F}_2$ in (1) to change slightly (by maximum of 1·5 per cent as mentioned above).

Because of the smallness of all these factors, we think it impossible, using the observations so far available, to prove that the rotating atmosphere can have an effect on the rotation of satellites, and even less provide evidence of strong winds in the upper atmosphere. From the theoretical point of view, an acceleration of the rotation as indicated in the last days of November (see Fig. 1) is only possible for periods exceeding about 100 sec., provided the position of the rotation axis is favourable.

It is quite certain that the observed period of flashing of 1958δ1 is not identical with its true rotation period[4,5]. An attempt to calculate the real period from the observed flashes has shown[6] that very great deviations up to about 0·9 sec. from the true period may occur, especially if the distance of the satellite from the observer is small (for example, July 1–25, 1958). A similar effect may be present at the end of November. Therefore it is not necessary to explain the behaviour of the rocket at that time by a real acceleration of its rotation. Unfortunately, it was not possible for us to determine the true period from the known observations in November, because

of the lack of a sufficient number of exactly known moments of single flashes.

P. Notni
H. Oleak

Sternwarte Babelsberg,
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[1] Faulkner, C. R., *Nature*, **187**, 926 (1960).
[2] King-Hele, D. G., in *Space Research*, edit. by Kallmann, H., 8 (North Holland Publ. Co., Amsterdam, 1960).
[3] Notni, P., and Oleak, H., *Veröffentl. d. Sternw. Babelsberg*, **13**, Heft 3 (1959). (R.A.E. Farnborough Lib. Trans. 868.) Also Heft 5 (1960).
[4] Zessewitch, W. P., in *Trans. Astro. Union*, **10**, 722 (1958). (Camb. Univ. Press, 1960).
[5] Zessewitch, W. P., *Bull. of Stations of Opt. Obs. of Art. Earth Satellites*, **7**, 3 (Moscow, 1959.) (in Russian).
[6] Notni, P., and Oleak, H., *Veröffentl. d. Sternw. Babelsberg*, **13**, Heft 4 (1959) (R.A.E. Farnborough Lib. Trans., 864).
[7] Moore, J. G., *Sky and Telescope*, **18**, 83 (1958).

My estimate of a decrease of 0·3 sec. in the rotation period (strictly the 'tumbling' period) is the residual effect, after making allowance for the difference between the flash period and the true rotation period. Observing from the north of Scotland, I found that by November 27–28, 1958, the flash period had fallen to 8·95 sec. in transits across the south-west at about 0·8°/sec.

I think it is possible to show that only about half the decrease can be attributed to more rapid movement of the observers' line of sight, if it is assumed that the number of flash cycles could never be more than one greater than the actual number of 'tumbles'.

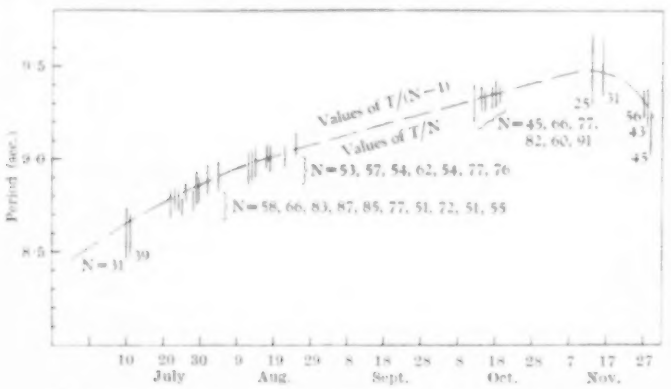

Fig. 1. Tumbling period of satellite 1958β1, estimated from observations of large numbers of flashes

In constructing Fig. 1, I have used only published observations[1,2] of large numbers of flashes. Each result gives an initial range of uncertainty as drawn between T/N and $T/(N-1)$, where T is the interval containing $(N+1)$ flashes.

The expression for the full rotation period:

$$P = 2T/(N - \theta/180)$$

gives consistent results, where θ is the angle of movement of the line of sight during an observation. The broken curve in Fig. 1 contains what appear to be essential features of the variation. Apart from timing errors, the true curve must pass through the tie-line joining T/N to $T/(N-1)$ for each observation, at a position depending on the value of θ, and therefore closer to $T/(N-1)$ when θ is large.

Any southern hemisphere observations (near epogee) during May or June 1958 would be a valuable check on the form of the early variation.

If it is accepted that a real change took place, at least in November, there follows the problem of finding an explanation. The idea of a 'cross-wind' introduces a non-symmetry of the correct kind, but I agree it should be stated relative to the satellite, and so represent the combined effect of rotation of the atmosphere and any westerly flow greater than the angular velocity of the Earth.

It seems necessary to seek an additional combination of deviations from, and extreme variations within, the ideal model used by P. Notni and H. Oleak in their very thorough analysis.

During an interval when the change in angle B is small, the braking moment Dp is controlled by ϱ, the air density at perigee. ϱ can be calculated from the height of perigee[3], the air density at that height[4], and the deviation from the mean experienced by this satellite[5].

From August until the end of October 1958, the increase of ϱ was small, and, apart from the 28-day period of solar disturbances, regular. During this period, the braking moment appears to have been constant. In November, ϱ increased at a greatly increasing rate, while my Fig. 1 represents an increasing acceleration of tumbling. The data are not accurate enough to prove that the increase of acceleration is proportional to the increase of air density, but an explanation of the changes can be advanced on this assumption.

This requires proof first of a mechanism to convert most of the air friction to accelerating torque, and second, a main braking force independent of the air density.

The acceleration might arise from large non-symmetries of shape and weight distribution in the rocket body, and a true windmill effect.

A precise evaluation of the contribution of magnetic damping may prove to be significant. For the case of a small rapidly rotating spherical satellite, Davis, Whipple and Zirker[6] found that the effect of air friction should be "several orders of magnitude less" than the expected damping of spin by the Earth's magnetic field. For 1958β1, there are factors of 500 in the rate of spin, and perhaps 10 in the ratio of axial length to diameter.

Note added in proof. I have not yet been able to study the discussion of magnetic retardation by Notni and Oleak in their ref. 6.

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HD 101065—a G0 Star with High Metal Content

On April 26, 1960, in the course of a spectroscopic survey of stars with large proper motions, a spectrum of the eighth magnitude star *HD* 101065 was observed with the Zeiss spectrograph at the Newtonian focus of the 74-in. telescope at Mount Stromlo Observatory. This star, classified as a *B5* star in the Henry Draper Catalogue, proved to be a much cooler star with a peculiar spectrum of unknown type. The spectral type of this star as estimated from the continuum, and later confirmed by three-colour photometry undertaken at my request by Mr. J. B. Whiteoak, is *K0*. The spectrum, however, shows strong hydrogen lines corresponding to class *F8* or *G0*. The assumption that this star may have a composite spectrum could not be substantiated by the appearance of the spectrum in the violet region since the strength of all Balmer lines uniformly corresponds to that of a *G0* star. The constant radial velocity of $+2{\cdot}3 \pm 1{\cdot}0$ km./sec. (based on three plates) and the six-colour photometry described here also suggest that the star *HD* 101065 is not a spectroscopic binary.

In view of the fact that no explanation could be found for the discrepancy between the spectral type determined from the continuum and from hydrogen lines (besides the obvious fact that the star in question has a peculiar spectrum) at my request this star was recently observed photoelectrically by Dr. G. E. Kron in six colours (private communication). The results of these observations are shown in Table 1 together with similar data for *HD* 19373—a normal main sequence *G0* dwarf, ι Persei[1]—and *HD* 140283—an extreme *G2* sub-dwarf (Stebbins, J., and Kron, G. E., private communication). Like the two other stars, *HD* 101065 is in all probability a dwarf, as the fairly high annual proper motion of 0·054″ and the six-colour photometry suggest. All three stars agree well in three colours, blue, green and red, and therefore should have essentially the same effective temperature not differing much from that of the Sun. If the difference in the infra-red is interpreted as a temperature effect the star *HD* 101065 should be the hottest and the sub-dwarf *HD* 140283 the coolest, but the difference should not be large. The three stars differ, however, considerably in their violet and ultra-violet colours. The sub-dwarf *HD* 140283, which according to L. H. Aller and J. L. Greenstein[2] and B. Baschek[3] contains only a negligible amount of metals in its atmosphere, possibly only 1/200 of the amount of metals in normal main sequence dwarfs, is the bluest, while the star *HD* 101065 is the reddest. The differences in the violet and ultra-violet are due to the differences in the degree of blanketing, that is, to the differences in the abundance of metals. The star *HD* 101065 should therefore have a much higher abundance of metal in its atmosphere than main sequence dwarfs. This is also suggested by the appearance of its spectrum, which contains about 500 lines, mostly unidentified, in the range λλ3922–4528 Å. on plates with a dispersion of 36 Å./mm. at $H\gamma$, taken with the three-prism spectrograph at the Cassegrain focus of the 30-in. Reynolds telescope.

The high abundance of metals is also suggested by the appearance of the continuum. It can be expected that the contribution of metals to the continuous absorption coefficient would suppress the continuum below 4300 Å. or possibly up to λ4400 Å., and therefore a high content of metals would change the continuum in the sense that the star would appear to be of a later type. Since the spectral type estimated from the continuum and from the three-colour photometry is *K0*, while the temperature of the star indicates a spectral type *G0*, the abundance of metals which would cause such a marked change in the appearance of the spectrum must be very high indeed. It is hoped that the spectroscopic study which I have started will provide in the near future a precise figure for the abundance of metals. I expect that the abundance of metals will prove to be many times higher than that of normal main sequence stars.

Table 1

Colour	*U*	*V*	*B*	*G*	*R*	*I*
λ in Å. / Star	3530	4220	4880	5700	7190	10,300
HD 140283	−0·52	−0·27	−0·04	−0·01	+0·03	+0·07
HD 19373	−0·16	−0·12	−0·03	−0·02	+0·05	+0·13
HD 101065	+0·08	+0·06	−0·04	−0·02	+0·07	+0·20

The energy distribution based on photoelectric spectrophotometry recently secured at my request by Prof. L. H. Aller will be described in another paper now in preparation. This paper will also contain a detailed description of the spectrum; the main features, however, are briefly noted here. The ionized calcium lines *H* and *K*, which are very prominent in normal *F* and *G* dwarfs and even in sub-dwarfs, are faint and approximately equal in strength to hydrogen lines. Also, the absorption spectrum of iron is greatly suppressed and only three lines of iron (λλ4045, 4063, 4071 Å.) can be seen beyond any doubt; the line at λ4045 Å. is fairly strong. The lines of ionized strontium at λ4077 Å. and of barium at λ4554 Å. on the contrary are considerably strengthened in comparison with normal dwarfs. The spectrum shows about 500 lines between λλ3922 and 4528 Å., the majority of which have not yet been identified. Preliminary identifications seem to suggest that many lines should be attributed to rare earths. The spectrum does not show any *G* band, which could be interpreted as an indication that the abundance of carbon is low.

The high abundance of barium and strontium—two elements with the magic number of neutrons in their nuclei—as well as the high abundance of rare earths indicate that the star *HD* 101065 is in an advanced stage of stellar evolution. The star apparently passed through a stage of evolution in which heavy elements were built up by slow neutrons. It presents the same evolutionary problems as *S* stars, complicated in addition by the fact that in all probability it is a dwarf.

I wish to thank Dr. G. E. Kron, who at my request observed the star *HD* 101065 in six colours in spite of the fact that this meant a loss of valuable observing time during his short stay on Mount Stromlo, J. Stebbins and Dr. G. E. Kron for their permission to use unpublished data on *HD* 140283, and Mr. J. B. Whiteoak for securing the *UBV* photometry of *HD* 101065 at a time when this could not be done by me.

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RADIOPHYSICS

The Total Electron Content of the Ionosphere during the Magnetic Disturbance of November 12–13, 1960

Measurements of the total electron content of the ionosphere by observation of the differential Faraday fading of lunar radio echoes on two closely spaced frequencies were first made by Evans[1]. Use of a transit aerial limited observations to 1 hr. per day and permitted only the mean diurnal variation of the total electron content (n_t) to be obtained. Similar measurements are now being made with equipment mounted on the 250-ft. Jodrell Bank radio telescope; this allows up to 16 hr. continuous observation a day and gives reliable information on short-term and day-to-day variations in n_t. The frequencies used are 100·60 and 99·40 Mc./s.

The present communication presents some results obtained during a magnetic disturbance during November 12–14, 1960. The sudden commencement preceding the main phase of the disturbance occurred between 12.00 and 15.00 hr. U.T. on November 12, and the most intense phase of the disturbance ($K > 7$) was between 18.00 hr. on November 12 and 15.00 hr. on November 13. Curves of n_t vs. time for each of the days November 11–14 are shown in Fig. 1 (full line). The periods covered are those when the Moon was at a high enough elevation to permit useful observations. The curves have been corrected to local mean time at the sub-ionospheric point, and the mean sub-ionospheric latitude is 50·0° N. Also shown in Fig. 1 are hourly values of the maximum electron density N_m (points) derived from f_0F2 values for Slough (51·5° N. geographic, 54·3° N. geomagnetic) and 3-hourly K indices for the Hartland Magnetic Observatory.

K was low throughout the observational periods on November 11 and 12, and the n_t curves for these two days are normal. The disturbance began shortly after moonset on November 12, and the n_t curve for November 13 covers a large part of the most intense phase of the disturbance. n_t is lower than normal during the pre-sunrise period, and also shows an abnormally low rate of increase after sunrise, so that its midday value is less than one-third of that on the two preceding days. N_m is unmeasurable at Slough from 19.00 on November 12 until 03.00 on November 13, and is abnormally low throughout November 13. Both n_t and N_m are very low in the pre-sunrise hours of November 14 and both have returned to their normal values by midday on this day. Aurora was visible almost overhead at Jodrell Bank shortly before moonrise on November 13, but had retreated to the northern horizon before observations began. Visual observations of aurorae in the British Isles for the night of November 12–13 (Paton, J., private communication) show that it is unlikely that an aurora was present in the line of sight to the Moon at any subsequent time.

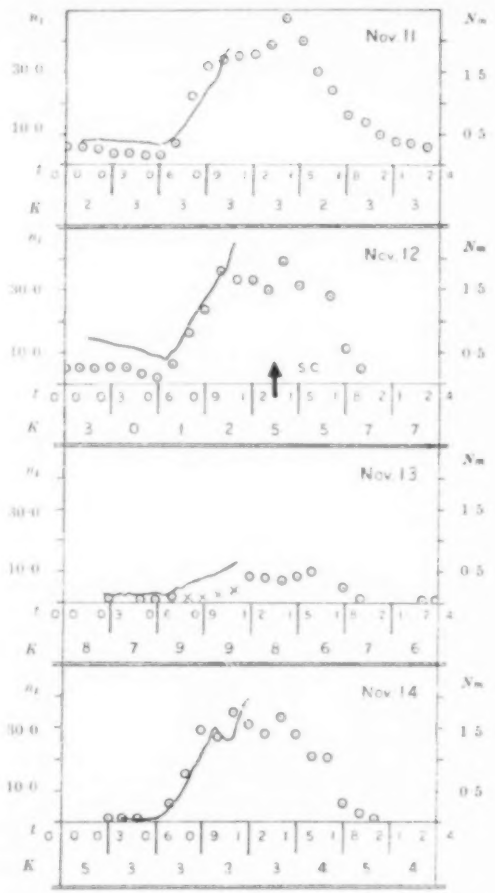

Fig. 1. Total electron content (n_t, full line) and Slough maximum electron density (N_m points) vs. time for each day during November 11–14, 1960. Also shown are Hartland K indices (K) and the approximate time of the sudden commencement on November 12 (s.c.). Upper limits are indicated as ×. Units: n_t, electrons/cm.² column × 10^{-12}; N_m, electrons/cm.³ × 10^{-6}; t, hr.

Table 1. Behaviour of Certain Parameters at Selected Time during November 11–14, 1960

	Nov. 11	Nov. 12	Nov. 13	Nov. 14
n_t at 05.00 L.M.T.* (electrons/cm.² × 10^{-12})	7·6 ± 1·3	10·9 ± 1·3	2·8 ± 2·1	0·8 ± 0·5
n_t at 10.00 L.M.T. (electrons/cm.² × 10^{-12})	33·8 ± 1·7	35·4 ± 1·7	9·6 ± 2·9	30·2 ± 1·4
dn_t/dt from 07.00 to 10.00 L.M.T. (electrons/cm.²/hr. × 10^{-12})	8·3	8·0	1·9	7·5
n_t/N_m at 05.00 L.M.T. (km.)	450 ± 80	570 ± 70	500 ± 300	200 ± 120
n_t/N_m at 10.00 L.M.T.	200 ± 10	200 ± 10	> 640	220 ± 10

* Local mean time.

The pre-dawn values of n_t are very low on both November 14 and 13; since magnetic activity was much lower at this period on November 14 than 13, the low value on the former date can probably be

Some relevant parameters for each of the four days are shown in Table 1. Listed here are n_t at 05.00 and 10.00 hr.; the mean rate of increase, dn_t/dt, between 07.00 and 10.00 hr.; and the equivalent column height, n_t/N_m, at 05.00 and 10.00 hr. The error in n_t is proportional to the error of measurement of the total number of Faraday rotations. This latter error is normally ± ½ rotation, and the corresponding errors in n_t are listed in Table 1. The errors shown for November 13 are rather larger than normal. This is partly because the Faraday fading on this day was slow and erratic throughout, and also because the record was partially obscured by interference for about an hour just before dawn.

attributed to normal night-time decay following a low noon maximum on November 13. The low value of dn_t/dt after dawn on November 13 suggests that one of the effects of the disturbance may be either an increased rate of recombination or a decreased rate of production of electrons in the lower levels of the ionosphere, where most of the ionization originates. The equivalent column heights at 05.00 hr. lie in the normal range on November 13 and November 14, but this parameter appears to be abnormally high at 10.00 hr. on November 13.

Several workers have measured n_t during magnetically disturbed periods by observations of transmissions of satellites. Hame and Stuart[2] report decreases in n_t at two periods of high magnetic activity near the vernal equinox. Ross[3] finds an inverse correlation between n_t and K_p, the correlation being good in the summer but poor in the winter. Garriott[4] finds normal values of n_t and abnormally high equivalent column heights on disturbed days, the observations applying mainly to the winter half of the year.

These results are not necessarily inconsistent with the present ones, since all the previous observations were made at appreciably lower geomagnetic latitudes than apply here. Maeda and Sato[5] have shown that, at high latitudes, ionospheric disturbances are mainly 'negative' in type (f_oF2 decreases) at all times of the year, while in medium latitudes disturbances are predominantly negative in summer, but may be either positive or negative in winter. The importance of the observations described in this communication is to show that, at least on the present occasion, the reduction in N_m was accompanied by a proportional reduction in n_t. Thus there appears to have been a scaling down of the whole ionosphere rather than a vertical redistribution of ionization within it.

I wish to thank Sir Bernard Lovell for the use of the facilities of the Nuffield Radio Astronomy Laboratories and Dr. J. H. Thomson for valuable guidance. Thanks are also due to the Director of the Radio Research Station (Department of Scientific and Industrial Research), Slough, and the Superintendent of the Magnetic Department, Royal Greenwich Observatory, for permission to quote pre-publication values of f_oF2 and K indices respectively. This work was carried out under U.S. Air Force Contract No. *AF*61(052)–172.

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PHYSICS

Optical Demonstration of Bragg's Law

A simple and rather striking demonstration of Bragg's Law can be given by making use of Lippmann's method for producing colour photographs[1]. In this method a photographic plate with an extremely fine-grained emulsion is placed with its sensitive layer on a mercury surface. It is then exposed from above, through the glass plate, to monochromatic light, for example from a sodium arc lamp. Due to reflexion at the mercury surface, standing light waves are produced in the sensitive layer, which, after development, give rise to parallel equidistant layers of photolytic silver, with a spacing equal to half the wave-length of sodium light.

Such a plate, of dimensions, for example, 3 cm. × 3 cm. (prepared in this Laboratory by B. Phielix, using, with some modification, a method described by H. Lehmann[2]), is fixed on a revolving holder, and inserted in an ordinary spherical glass flask as used in chemical experiments (diameter about 10 cm.). The flask is filled with benzene, to prevent reflexion at the outer surface of the emulsion layer. If now a parallel beam of white light, after passing through the solution, is reflected by the Lippmann plate, the latter acts as an 'interference mirror', and reflects a coloured beam, the colour changing with the angle of incidence. The reflected beam, when falling on a transparent screen, is of sufficient strength to be visible in a lecture room. In the experiment as I have performed it, the colour changes from yellow at a glancing angle θ in the neighbourhood of 90° to violet at θ about 45°.

The arrangement may serve to illustrate the influence of a slight change in spacing on the reflected wave-length. By breathing on the sensitive layer, a slight swelling of the gelatine takes place, which produces a considerable change in colour, from yellow to red for θ close to 90°, whereas for $\theta \sim 45°$ the colour of the reflected beam changes only from violet to blue. Thus also the different sensitivity of 'high-angle' and 'low-angle' reflexions for a slight change in spacing can be illustrated.

I do not know whether this 'application' of Lippmann's plates has already been described elsewhere. In a most interesting paper on "The Crystal Structure of *Tipula* Iridescent Virus as determined by Bragg-Reflection of Visible Light"[3], A. Klug, (the late) Rosalind E. Franklin and S. P. F. Humphreys-Owen analysed a crystal with lattice spacings so large that these could be measured by reflexion of visible light. Dr. Klug told me that cells containing these virus crystals had been used to demonstrate Bragg's law optically. This suggested to me that the above demonstration might be of some interest.

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Acceleration of Deuterons in a Synchrotron

Because of the theoretical interest in the study of the collisions between nucleons, all the large heavy-particle synchrotrons at present operating have been designed to accelerate protons[1]. In many of these machines, however, the frequency of the accelerating voltage can be pre-set to follow any suitable law of variation with magnetic field. There is nothing then to prevent the acceleration to an appropriate energy of particles with an e/m different from that of the proton providing that they can be injected.

In the Birmingham proton synchrotron[2] the radio-frequency law was originally obtained by a rotating condenser which varied the capacity in an oscillator circuit[3]. This system has now been successfully

replaced by an analogue computer and a function generator, driven by a signal proportional to the rate of change of magnetic field, the output signal controlling a variable capacitance diode in an oscillator circuit. This allows considerably greater flexibility. The low injection energy and small aperture of the Birmingham machine impose severe limits on the permissible errors of the radio-frequency at injection. As a result, the system requires a signal to noise (and drift) ratio of $10^3:1$, and this has been achieved. It has been found possible to accelerate deuterons readily with this installation.

Deuterium gas was supplied to the radio-frequency ion source of the synchrotron injector. With the same injection energy as for protons (460 keV.) a beam was found to enter the synchrotron vacuum system and to circulate before acceleration at a magnetic field of $\sqrt{2}$ times the value for protons. This beam was carried to full energy (estimated from the magnetic field to be 642 ± 12 MeV. for mass 2) by suitable adjustment of the radio-frequency function generator and was found to circulate at maximum field with a frequency 0·76 times that for protons. The beam was extracted from the synchrotron by the method normally used for protons[4] and was found to have an intensity of 10^8 particles per pulse over an area of 12 cm.^{2} at a distance of 16 m. from the extractor. The range of the beam in copper was measured to be 167 ± 3 gm. cm.$^{-2}$ which, allowing for 7-MeV. energy-loss in polythene and air in the beam path, corresponds to an energy of 640 ± 5 MeV., confirming that the particles accelerated were deuterons. No beam was accelerated when hydrogen gas was fed to the ion source with the radio-frequency generator set for deuterons.

The identity of the accelerated particles was also confirmed in a preliminary experiment to measure the differential cross-section for the elastic scattering of deuterons by protons. Coincidences between scattered deuterons and recoil protons from a hydrogenous target were recorded at the correct correlation angle; when the counter telescopes were moved off this angle the counting-rate dropped to 20 per cent of that previously obtained. It is hoped to continue these observations and to extend them to a study of the deuteron–deuteron interaction at the available energy.

The new radio-frequency installation was developed from a system proposed by W. Boyd and his team at the National Institute for Research in Nuclear Science, Harwell. We wish to acknowledge the valuable help we have received from them at all stages of the work. We are also indebted to D. A. Gray of the Institute for assistance in the problem of deriving signals from the rising magnetic field. Many members of the synchrotron group of this laboratory also contributed to this project, in particular K. R. Chapman, who made the necessary adjustments to the ion source, and the Counter Group, who made the range and scattering measurements.

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The Quasi-Longitudinal Approximation to the Appleton–Hartree Equation

If an electromagnetic wave passes through a medium containing free electrons, which may make collisions with heavy particles, in the presence of a uniform magnetic field, the refractive index and absorption coefficient of the medium are given by the Appleton–Hartree equation[1]:

$$\mu^2 = (\mu - i\chi)^2 = 1 - \frac{X}{1 - iZ - Y_T^2/2(1 - X - iZ) \pm [Y_T^4/4(1 - X - iZ)^2 + Y_L^2]^{1/2}} \quad (1)$$

where μ = refractive index; χ = absorption coefficient; $X = f_0^2/f^2$; $Y_T = (f_H/f)\sin\theta$; $Y_L = (f_H/f)\cos\theta$; $Z = \nu/2\pi f$; f = frequency of wave; f_0 = plasma frequency; f_H = gyrofrequency; ν = frequency of collisions between electrons and neutral molecules; θ = angle between wave normal and magnetic field.

Because of the complicated nature of the above equation the quasi-longitudinal and quasi-transverse approximations, first discussed by Booker[2], are often used.

The quasi-longitudinal approximation holds when:

$$Y_T^4/4Y_L^2 \ll (1 - X)^2 + Z^2 \quad (2)$$

It is generally quoted as:

$$\mu^2 = 1 - X/(1 - iZ \pm |Y_L|) \quad (3)$$

Equation (3) means that the wave behaves very much as if it is being propagated along the direction of the magnetic field, since, for longitudinal propagation, equation (1) reduces to:

$$\mu^2 = 1 - X/(1 - iZ \pm Y) \quad (4)$$

However, equation (3) is incorrect, as can easily be seen by considering the denominator of the second term of equation (1):

$$1 - iZ - Y_T^2/2(1 - X - iZ) \pm [Y_T^4/4(1 - X - iZ)^2 + Y_L^2]^{\frac{1}{2}}$$

When the inequality (2) holds, this becomes:

$$1 - iZ - Y_T^2/2(1 - X - iZ) \pm |Y_L|$$

and $Y_T^2/2(1 - X - iZ)$ is not necessarily negligible compared with Y_L. In fact, if we assume the usual numerical condition that the inequality (2) is satisfied if the larger quantity is nine times the smaller, then $|Y_T^2/2(1 - X - iZ)|$ may be as large as $\frac{1}{4}Y_L$. The correct approximation is thus:

$$\mu^2 = 1 - \frac{X}{1 - iZ - Y_T^2/2(1 - X - iZ) \pm Y_L} \quad (5)$$

and the wave does not behave as if it were propagated along the direction of the magnetic field. It will only behave thus when the term $Y_T^2/2(1 - X - iZ)$ can be neglected, that is, when:

$$Y_T^2/2Y_L \ll |(1 - X) - iZ| \quad (6)$$

Outside these limits, but where inequality (2) still holds, equation (5) should be used. A similar correction should also be made to the expressions for the polarization.

I am grateful to Prof. J. A. Gledhill for some helpful discussion.

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MINERALOGY

Kilchoanite, a Polymorph of Rankinite

THE compound $9CaO6SiO_2H_2O$ was originally synthesized and described by Roy[1,2], who called it phase *Z*. Revised data on its properties have been given by Roy, Gard, Nicol and Taylor[3], who showed that, when hydrothermally synthesized at 715° C. and with a pressure of 1,100 bars, its composition was $3CaO2SiO_2$ and that it became inverted to rankinite on heating between 954° C. and 1,090° C.

A mineral corresponding to phase *Z* has been found in limestones thermally metamorphosed by gabbro at Ardnamurchan, Scotland, and Carlingford, Eire. It has been named kilchoanite after the village in Ardnamurchan near where it was first found.

It has the following properties: colourless, slightly turbid due to minute inclusions and no visible cleavage, α 1·647, γ 1·650, $\gamma - \alpha$ 0·003, $+$ 21° 60′, dispersion distinct $r > v$, density 2·992. In thin section the interference colours are commonly weak ultra-blue and ultra-brown.

Kilchoanite has always been found as a replacement of rankinite and no crystal form has been observed. Single crystal X-ray data indicate that it is orthorhombic with a 11·42 Å., b 5·09 Å., c 21·95 Å. (all ± 0·05 Å.). The Laue group is *mmm* and the probable space group *I mam* or *I ma*2. X-ray powder data, given in Table 1, agree with those of Roy[3] for the phase *Z* apart from discrepancies which could be due to impurities in the latter.

Separation of kilchoanite for analysis was difficult owing to the complexity of the mineral assemblages with which it is associated and because of its irregular distribution. A rock containing no rankinite was eventually used to prepare a sample in which spurrite was the only impurity. Having established that kilchoanite contained no carbon dioxide, this sample was analysed. On the assumption that all the carbon dioxide was in the contaminating spurrite, this analysis, together with the cell dimensions and the determined density, gave the calculated cell contents as:

$$(Ca_{23\cdot47}Mn_{0\cdot03}Fe^{III}_{0\cdot05})_{23\cdot55}(Si_{15\cdot71}Al_{0\cdot25})_{15\cdot96}(O_{55\cdot53}OH_{0\cdot47})_{56\cdot00}$$

This value is in close agreement with $8(Ca_3Si_2O_7)$ and confirms that kilchoanite corresponds to the phase *Z* and is a polymorph of rankinite. Further confirmation is found in that on heating at 1,000° C. for 10 hr. a single crystal of kilchoanite became inverted to a polycrystalline aggregate of rankinite.

The metamorphic assemblages from which kilchoanite is developed consist essentially of:

rankinite—spurrite—melilite
rankinite—wollastonite—melilite

These give way to assemblages such as:

rankinite → kilchoanite — spurrite → tilleyite — melilite — cuspidine
kilchoanite — tilleyite — melilite — cuspidine
kilchoanite — spurrite — grossular — idocrase — cuspidine
kilchoanite — wollastonite — grossular — idocrase

It is suggested that kilchoanite does not form in normal prograde metamorphism as under conditions of relatively high carbon dioxide pressure the reaction spurrite + wollastonite → rankinite + carbon dioxide, is above the stability limit of kilchoanite. If, however, the rock has been decarbonated, a later retrograde phase or repeated thermal metamorphism under a low carbon dioxide pressure may convert the rankinite to kilchoanite at lower temperatures in the presence of water.

Further work on this mineral and these rocks is in progress and will be reported in detail later.

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CRYSTALLOGRAPHY

Etch Patterns on Cadmium Crystals grown from Vapour

SERVI[1] showed complex spirals on the basal plane of cleaved zinc crystals after etching, and spiral terraced etch pits have been obtained on zinc crystals[2] grown from vapour using 'Superoxol' etch. Presented here are two types of etch figures obtained on 99·9 per cent cadmium crystals grown from vapour. Of several etching reagents that had been tried the most suitable one was a saturated solution of picric acid in acetone and a normal time of 2 min. was decided on. For longer periods of etching the solution acted as polishing agent.

Table 1

Kilchoanite d_{hkl}	I	d_{hkl}	Phase *Z* I	$d_{calc.}$	hkl	Kilchoanite d_{hkl}	I	d_{hkl}	Phase *Z* I	d_{calc}	hkl
5·17 Å.	*m*	5·10 Å.	0·2	5·07 Å.	202	2·26	*vw*	2·26	0·05	2·27	222
—	—	4·76	0·1	—	—	2·18	*vw*	—	—	—	—
4·26	*w*	—	—	4·28	112	2·06	*w*	—	—	—	—
—	—	4·18	0·1	4·18	013	1·996	*w*	—	—	—	—
4·00	*w*	3·97	0·2	3·97	204	1·964	*ms*	1·961	0·3	—	—
—	—	3·76	0·1	3·74	211	1·906	*m*	1·902	0·15	—	—
—	—	3·67	0·1	3·66	006	1·872	*m*	—	—	—	—
3·56	*ms*	3·56	0·4	3·54	114	—	—	1·823	0·3	—	—
3·39	*vw*	—	—	3·37	213	1·814	*w(b)*	—	—	—	—
3·07	s_4	3·06	0·75	3·08	206	1·779	*w*	—	—	—	—
				3·05	310	1·745	*m*	1·749	0·2	—	—
2·89	s_1	2·88	1·0	2·88	116	1·694	*m*	1·692	0·1	—	—
				2·87	215	1·659	*vw*	—	—	—	—
—	—	2·84	0·3	2·86	400	1·602	*w*	—	—	—	—
2·77	*vw*	—	—	2·76	402	1·569	*vw*	1·570	0·05	—	—
—	—	2·73	0·1	2·74	008	1·559	*w*	—	—	—	—
2·68	s_3	2·67	0·75	2·69	017	1·548	*w*	—	—	—	—
				2·67	314	1·526	*m*	—	—	—	—
2·55	*m*	2·55	0·2	2·55	020	1·487	*w*	1·489	0·05	—	—
2·48	*m*	2·48	0·2	2·48	121	1·418	*m*	—	—	—	—
				2·48	411	1·398	*vw*	—	—	—	—
2·42	*m*	2·42	0·3	2·43	217	1·379	*vw*	—	—	—	—
2·36	*ms*	2·35	0·15	2·36	118	1·357	*vw*	—	—	—	—
				2·35	123	1·337	*vw*	—	—	—	—
—	—	—	—	2·34	316	1·332	*w*	—	—	—	—

etc.

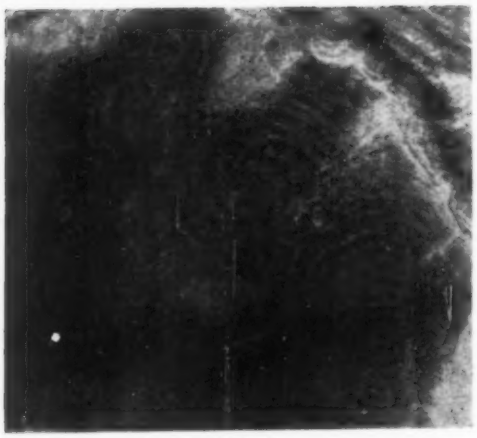

Fig. 1

Fig. 2

Several complex spirals were observed on the basal planes of some of the crystals after etching (Fig. 1). The hexagonal symmetry of the basal plane is clearly indicated in these spirals. This suggests that crystal symmetry is a factor in etch spiral formation. As the spiral moves outwards it breaks up into terraces, and a sort of interlacing occurs. It is interesting to note that the spirals break and make along crystallographic directions. In some cases etch patterns closely resembling hexagonal spirals with the dislocation line emerging at the centre were observed (Fig. 2). It is evident that these etch pits are formed at the sites of dislocations.

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GEOLOGY

Palæoecology of Carboniferous Peat Bogs

The microscopic examination of coals can provide valuable information on their mode of formation. The works of Teichmüller[1] and Thomson[2] on the Rhineland brown coal are notable examples. Apart from the investigations of Kremp[3] and Smith[4], little of the published work on the possible origin of the different petrographic types of coal takes account of the evidence provided by the plant spores in coals of Carboniferous age.

Recently, a systematic study of the petrology and palynology of British bituminous coals from the Lower and Middle Coal Measures of the East Pennine coalfield has yielded results which are not only of theoretical importance, but also provide information which will permit the more effective use of spores in the correlation of coal seams. These results are being prepared for publication.

Broadly speaking, each of the more important petrographic coal-types possesses a distinctive assemblage of miospores (and probably megaspores). Four main types of assemblage have been recognized, associated respectively with predominantly bright, interbanded, and the two distinct petrographic types of dull, coal. These assemblages are related in the order in which they succeed one another in seam profiles. A full sequence is found only in seams containing dull coal characterized by the petrographic constituents micrinite (massive) and exinite, the latter largely comprising the exines of a single spore *Densosporites sphaerotriangularis* Kos. A sequence may be repeated more than once within a seam profile.

It is possible to recognize, within the profiles, horizons with distinctive petrological and palynological features which include allochthonous elements. These horizons probably mark the flooding of the bog surface and their occurrence may modify the development of a sequence.

From what is known of the botanical affinities of the spores, it is possible to visualize something of the nature of the plant succession corresponding to the sequence of miospore assemblages. The conditions under which peat formed may be inferred from the nature and possible origin of the petrographic constituents associated with the different assemblages of spores.

Any hypothesis as to the conditions under which peat was formed in the Carboniferous must take account of the evidence provided by work on the frequency and stratigraphic ranges of spores found in the seams in all the major British coalfields. These have demonstrated an essentially identical pattern of distribution and abundance in the different coalfields. Also to be considered is the occurrence, over wide areas within a coalfield, of beds, often nearly constant in thickness, of dull coal containing massive micrinite and spores predominantly of one type. This petrographic type is known from coals of paralic and limnic origin, and is a conspicuous feature of the middle and upper portions of certain seams in the Lower and Middle Coal Measures in Britain.

With regard to the palynological evidence, it is thought unlikely that the quantitative and qualitative composition of the miospore assemblages from whole seams of coal deposited contemporaneously would show common features if depth of water cover or salinity had been the controlling factor determining the nature of the vegetation growing in the areas of peat deposition. Considering those features of the dull coal to which reference has been made, W. G. Chaloner (personal communication) suggested that the formation of peat of a distinctive type within certain Carboniferous bogs may have taken place under conditions similar to those which give rise to blanket bogs at the present time, and that the causative factor was more likely to be a climatic (for example, rainfall) fluctuation than simply one of water-level.

Such a mode of origin accords well with the observed facts. By analogy with present-day raised bogs, it seems reasonable to suggest that the vertical changes which took place as peat accumulated in these Carboniferous deposits may have been the result of the increase in acidity and the decrease in nutrients available for plant growth. On this view, therefore, the sequences which have been observed may mark the change from peat of eutrophic to that of oligotrophic type.

It is of interest that the study of the peat deposits of north-west Borneo by Andrews and Richards[5] suggests that these peats are of raised-bog type. The vegetation growing on these peats is arboreal and is reported to exhibit a concentric zonation. Profiles from the central parts of the deposit show a succession of peat types formed from the same plant communities that occur at the present time from the periphery to the centre. In this and other respects there is probably a close analogy with the structure observed in certain coals which originated in Carboniferous peat bogs.

The mode of peat formation, which it is suggested might account for the petro-palynological characteristics of certain Carboniferous coal seams, is different from that postulated by Teichmüller[6] for the brown coals of the Rhineland.

The possible climatic control of bog structure in the Carboniferous would explain features of the distribution and abundance of miospores in coal seams of the period.

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CHEMISTRY

Polymers and the Theory of Numbers: Molecular Weight Distributions from Rheological Measurements

Recently, V. S. Nanda and R. K. Pathria have shown how certain problems from the theory of numbers may be applied to the theory of polymer degradation[1]. Their work appears to be one of the very few applications of the theory of numbers to physical or chemical problems. We wish to report a new application of another classical theorem of the theory of numbers to yet another problem in the field of polymer physical chemistry. By the use of this theorem, it appears to be possible to obtain the molecular weight distribution of a polymer sample from rheological measurements.

Rouse's equation[2] for the real part of the complex viscosity of a polymer solution may be written as:

$$\eta_1(\omega) = K \sum_{p=1}^{x} f(\omega/p^2) \qquad (1)$$

where η_1 is the real part of the complex viscosity, ω is the frequency and K is a frequency-independent parameter.

The function $f(\omega/p^2)$ is a type of Stieltjes transform of the molecular weight distribution function, $Z(M)$, defined as $MW(M)/\overline{Mw}$, where $W(M)$ is the weight fraction of polymer between molecular weights M and $M + \mathrm{d}M$, and $\overline{Mw}$ is the weight-average molecular weight. In fact, $Z(M)$ is related to $f(\omega) \equiv f(\omega/1^2)$ by the relation:

$$Z(M) = \mathscr{S}\{f(\omega)\} \qquad (2)$$

where $\mathscr{S}$ stands for inversion of the Stieltjes transform. Such an inversion may be obtained to any desired approximation through the use of the inversion formula of Hirschman and Widder[3]. In order to obtain $f(\omega)$ from equation (1), we use the classical number-theory theorem of Moebius[4] to obtain:

$$f(\omega) = K^{-1} \sum_{s=1}^{\infty} \frac{\mu_s}{s^2} \eta_1(\omega/s^2) \qquad (3)$$

where μ_s is the Moebius μ-function defined as equal to $+1$ if s is $+1$ or if s can be factorized into an even number of unlike primes and -1 if s can be factorized into an odd number of unlike primes, and zero for other values of s. Combining (2) and (3), we have:

$$Z(M) = \mathscr{S}\left\{K^{-1} \sum_{s=1}^{\infty} \frac{\mu_s}{s^2} \eta_1(\omega/s^2)\right\} \qquad (4)$$

Thus if $\eta_1(\omega)$ is known experimentally for any polymer, equation (4) gives an equation for directly obtaining the molecular weight distribution function. The potential usefulness of such a relation lies in the fact that it may present a far easier and more rapid method of experimentally determining the molecular weight distribution of a polymer than has heretofore been possible.

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The BH_4^- Ion in the Lithium Borohydride Lattice

Price[1] reports an anomalous band at about 1,250 cm.$^{-1}$ in the paraffin-oil mull spectrum of lithium borohydride at room temperature. This band does not occur in the room-temperature spectra of sodium borohydride[2,3] and potassium borohydride[3] or in the low-temperature spectra of sodium borohydride[2,4] and potassium borohydride (Schutte, C. J. H., unpublished results).

The crystal structure of lithium borohydride is orthorhombic (space-group V_h^{16}) with four molecules per unit cell[5].

V_h^{16} has the following sites[6]: $2C_s(4)$ and $C_s(4)$. A comparison of the site groups of the space group and the sub-groups of the ionic point group (T_d) shows that the BH_4^- ion is on site C_s. The local-symmetry group of the ion, constructed from the common elements of the site group and the space group, is C_{2v}.

The symmetry of the perturbing crystal field acting on the tetrahedral BH_4^- is thus C_s. Under the action of a perturbing field of symmetry C_s the vibrational levels of the tetrahedral ion transform as follows:

$$\begin{array}{ccc} T_d & & C_s \\ A & \rightarrow & A' \\ E & \nearrow & A' \\ & \searrow & A'' \\ F_2 & \nearrow & A'' \\ & \rightarrow & A' \\ & \searrow & A' \end{array}$$

that is, the degeneracy of all the levels is removed and all the levels are infra-red active (only the F_2 levels are infra-red active under T_d).

This means that all four tetrahedral fundamentals should be observable in the infra-red absorption spectrum, as well as all the overtones and combination bands. In addition, all the degenerate bands should show fine structure caused by the removal of all the degeneracy by the perturbing crystal field.

The splitting of the degenerate bands would probably be obscured by the broadness of the bands at room temperature, but ν_1 and ν_2 should be observable. Unfortunately, the band due to the ν_1 vibration lies among ν_3 and its satellite bands (at about 2,300 cm.$^{-1}$) and could easily be obscured by these.

From the spectrum published by Price[1] it can be deduced that ν_2 should occur around 1,280 cm.$^{-1}$ (from the frequencies of ν_4 and $\nu_3 - \nu_4$).

The anomalous band reported by Price[1] at about 1,250 cm.$^{-1}$ in the spectrum of lithium borohydride can thus probably be assigned to the ν_2 vibration of the BH_4^- ion in the lithium borohydride lattice. This band is normally inactive in the infra-red, but occurs here because of the 'reduction' of the symmetry of the ion by the crystalline field, which is of the type C_s.

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Isolation of D-Glycero-D-galacto-heptitol from the Wound Exudate of Avocado Trees

D-Glycero-D-galacto-heptitol has been isolated from the semi-crystalline exudate of wounds in the bark of *Persea americana* Mill.

The crude material was a pale brown solid which did not reduce Fehling's solution, and gave evidence of only one major component on paper chromatograms. Two recrystallizations of this solid from aqueous methanol afforded a colourless product in the form of needles which had a melting-point of 183–185°, no depression on admixture with authentic perseitol.

A portion of the crude exudate was acetylated with pyridine and acetic anhydride to give a crystalline acetate, which after recrystallization from aqueous ethanol had a melting-point of 119–120·5°, no depression on admixture with authentic perseitol heptaacetate. This derivative also had $[\alpha]_D^{22°} - 14°$ (about 2·02 in chloroform); literature value[1] $[\alpha]_D^{20°} - 13·3°$ (chloroform).

A further portion of the crude material was treated with benzaldehyde and acid according to Hudson *et al.*[2]. From this reaction mixture a crystalline derivative was isolated, which after one recrystallization from pyridine–ethanol had a melting-point of 276–278° and $[\alpha]_D^{22°} - 62°$ (about 1·95 in pyridine). Hudson *et al.*[2] give values of 277 ± 2° for the melting-point and $[\alpha]_D^{20°} - 58·1°$ (about 0·9 in pyridine) for 1,3 : 5,7-di-O-benzylidene-D-glycero-D-galacto-heptitol.

From these results we have concluded that the chief constituent of *Persea americana* Mill wound exudate is D-glycero-D-galacto-heptitol (perseitol), a compound known to be present in the fruit[3] and leaves[4] of this tree.

Thanks are due to Drs. L. W. Klotz and G. A. Zentmyer of the Citrus Experiment Station, Riverside, California, who supplied the exudate described here.

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Monosaccharide Sequence in *Pneumococcus* Type XIV Polysaccharide

Previous work[1] has established that in *Pneumococcus* type XIV polysaccharide there are two non-reducing end groups of D-galactopyranose, one D-galactopyranose residue linked 1 : 3, one D-glucose residue linked 1 : 4 and two 1 : 4 : 6-linked 2-acetamido 2-deoxy D-glucose residues for every six monosaccharide units. Although the majority of these linkages are β-, some α-D-galactose units may be present. The two major disaccharides left after treatment of the type XIV polysaccharide with *N* hydrochloric acid at 100° for 2½ hr. were 4-O-β-D-glucosyl 2-acetamido 2-deoxy D-glucose and 3-O-β-(2-acetamido 2-deoxy)-D-glucosyl D-galactose. Less drastic hydrolysis has enabled other disaccharides to be isolated and the structure of these is the subject of the present communication.

The polysaccharide (3·606 gm.) was hydrolysed with 2 *N* sulphuric acid (430 ml.) at 85–90° C. for 2½ hr. After neutralization with barium carbonate, the hydrolysate was passed through 'Amberlite *IR*' 120 (H^+), which was eluted with water to yield neutral sugars (1·8 gm.) and with 2 *N* sulphuric acid to remove basic sugars (1·0 gm.). Fractionation of the neutral sugars on a charcoal–'Celite' column[2] gave a D-galactose–D-glucose mixture (about 1·4 gm.), N-acetylglucosamine (40 mgm.), disaccharides I and II (4 mgm.), III (11 mgm.), V (30 mgm.), VI (3 mgm.), trisaccharides IV and V (30 mgm.), as well as trisaccharide VI and another oligosaccharide (30 mgm.).

The basic sugars were selectively N-acetylated[3] and fractionated on a charcoal–'Celite' column[2] to yield a D-galactose–N-acetylglucosamine mixture (0·80 gm.), disaccharides IV (9 mgm.), V (20 mgm.), trisaccharides I (6 mgm.), II (3 mgm.), III (12 mgm.) and higher oligosaccharides (24 mgm.). Disaccharides and trisaccharides are numbered in order of elution from the charcoal–'Celite' column.

Acid hydrolysis of disaccharide III (1 mgm.) and paper chromatographic analysis of the products showed that III contained D-galactose and D-glucose. Reduction of III with sodium borohydride afforded a disaccharide alcohol the components of which were D-galactose and sorbitol. Hence III was a galactosyl-glucose. III showed on paper chromatograms $R_{glucose}$ values of 0·33 in butanol/acetic acid/water (40 : 10 : 50), 0·45 in amyl alcohol/pyridine/water (1 : 1 : 1) and on paper ionophoretograms[4] an M_G value of 0·37 in borate buffer *p*H 10. In each case this behaviour was identical with that of lactose, and III is therefore 4-O-β-D-galactopyranosyl-D-glucose.

The mixture of disaccharides I and II was separated ($R_{glucose}$ values 0·26 and 0·33 respectively) on paper chromatograms irrigated with an amyl alcohol/pyridine/water (1 : 1 : 1) mixture. Acid hydrolysis of II gave D-glucose and D-galactose. Disaccharide II alcohol contained glucose and dulcitol. Since D-galactose must therefore occupy the reducing position in the disaccharide and previous methylation data[1] had established only 3-substituted galactose units, disaccharide II must be 3-O-β-D-glucosyl D-galactose. Its high mobility (M_G 0·70) on borate ionophoresis[4] supports this contention. Disaccharide I contained only D-galactose. Hydrolysis of disaccharide I alcohol gave galactose and dulcitol. Its high mobility (M_G 0·82) on borate ionophoresis[4] supports the assignment of its structure as 3-O-D-galactosyl-D-galactose.

Similar structural investigations established that disaccharides V and IV were identical with 4-O-β-D-glucosyl-2-acetamido 2-deoxy D-glucose and 3-O-β-(2-acetamido 2-deoxy)-D-glucosyl-D-galactose, which had been encountered in previous work[1]. Since the small amounts of disaccharides isolated might have arisen via acid reversion, a control experiment was carried out in which a synthetic mixture of D-galactose, D-glucose, and N-acetyl D-glucosamine (3 : 1 : 2) was submitted to the identical conditions of acid hydrolysis, etc., used in the hydrolysis of the polysaccharide. Only one disaccharide was detected, and this corresponded to disaccharide VI.

Trisaccharide VI ($R_{glucose}$ 0·20 in butanol/acetic acid/water; 0·28 in amyl alcohol/pyridine/water; M_G 0·10 in borate buffer) contained galactose, glucose and N-acetylglucosamine. Partial acid hydrolysis gave as well as these sugars the disaccharides III and V. Sodium borohydride reduction of trisaccharide VI and subsequent partial acid hydrolysis gave galactose, glucose and disaccharide III as the only reducing sugars. Hence trisaccharide VI is probably O-β-D-galactosyl-(1→4)-O-β-D-glucosyl-(1→4) D-(2-acetamido 2-deoxy)-glucose. Trisaccharides IV and V also contained galactose, glucose and N-acetylglucosamine as their component monosaccharides.

Although the fine details of the structure of type XIV polysaccharide must still await the characterization of other trisaccharides and higher oligosaccharides, the following points are significant with respect to the cross-reactivity of anti-type XIV *Pneumococcus* sera and various polysaccharides. Both human blood group A substance[5] and type XIV polysaccharide contain the disaccharide 3-O-β-(2-acetamido 2-deoxy)-D-glucosyl-D-galactose. Anti-type XIV sera do not react with intact A substance, but do so after treatment with acetic acid. Intact human Le^a blood group substance probably cross-reacts with anti-type XIV sera solely because of the presence of non-reducing end groups of D-galactose, since Watkins and Morgan[6] have concluded from inhibition studies that such terminal β-D-galactosyl groups are attached to the 3 position of neighbouring N-acetylglucosamine residues. No evidence has been found for the presence of 4-O-β-D-galactopyranosyl N-acetylglucosamine, which has been found[7] in pig group A substance and is believed by Schiffman, Howe and Kabat[8] to be responsible for cross-reactivity with anti-type XIV sera. The detection by us of 3-O-D-galactosyl D-galactose in type XIV polysaccharide is consistent with the presence of this disaccharide in lung galactan and other polysaccharides containing galactose which cross-react[9–11] with anti-type XIV sera. However, the cross-reaction of guar gum[12] with anti-type XIV sera appears to be due to the non-reducing α-D-galactose terminal units in this polysaccharide.

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BIOCHEMISTRY

Role of Tocopherol, Selenium and Anti-oxidants in the Rat

The view that α-tocopherol functions solely as a lipid anti-oxidant has long been implicit in the conclusions of many workers (Dam[1] has given a useful summary) and has again been most recently elaborated in the work of Zalkin and Tappel[2]. Other workers, however, have postulated a more specific role for tocopherol in animal tissues. We have already shown[3,4] that α-tocopherol and selenium both control ubiquinone-levels in the rat, and wish briefly to report here some work that provides strong evidence for a specific biochemical function of tocopherol, distinct from that of other lipid anti-oxidants.

Groups of six weanling female rats were reared for 10–12 weeks on a vitamin E-deficient diet. Some groups received throughout this period dietary supplements of 0·01 per cent *dl*-α-tocopheryl acetate, or 0·1 p.p.m. of selenium (as selenite) or 0·10 per cent of 'Santoquin' (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline). Other groups were given 80 mgm. of 'Santoquin' or 10 mgm. of α-tocopheryl acetate 48 hr. before all groups were killed. Tissues were analysed for ubiquinone and tocopherol by previously described methods[5]. Table 1 shows that, whereas tocopherol and selenium (which usually increased tissue tocopherol-levels) markedly increased ubiquinone in heart and liver, 'Santoquin' was inactive. Similar effects were found in other tissues.

Table 1. Effect of α-Tocopherol (α-Toc.), Selenium and 'Santoquin' on Ubiquinone (UQ) in Rat Tissues

Group and treatment	Heart		Liver	
	UQ (μgm./gm.)	α-Toc. (μgm./gm.)	UQ (μgm./gm.)	α-Toc. (μgm./gm.)
Control	144	1·8	62	0·7
+ 0·01 per cent α-Toc.	170	44·5	92	41·9
+ 10 mgm. α-Toc. dose	165	12·6	83	30·0
+ 0·10 per cent 'Santoquin'	128	1·4	68	6·5
+ 80 mgm. 'Santoquin' dose	151	1·3	65	6·6
+ 0·1 p.p.m. selenium	195	3·2	93	6·3

Table 2 illustrates another experiment. Four groups of 8 female rats were reared on the deficient diet to 4 months of age. One group received a dietary supplement of 0·05 per cent DPPD (*N*,*N*′-diphenyl-*p*-phenylenediamine), two other groups dietary 'Santoquin' (at either 0·015 or 0·10 per cent). The animals were killed and livers analysed for ubiquinone and vitamin A. At the same time, *in vitro* peroxide production was measured on three individual livers from each group of the thiobarbituric acid reaction[6], after incubating homogenates for 15 min. at 37°. Optical densities were recorded directly. Both *N*,*N*′-diphenyl-*p*-phenylenediamine and 'Santoquin' effectively protected vitamin A (increased liver storage) and both significantly prevented *in vitro* peroxidation in liver. Neither substance significantly increased ubiquinone in heart or liver.

Table 2. The Effect of 'Santoquin' and DPPD on Ubiquinone (UQ) and Vitamin A in the Rat, and their Protective Action on Peroxidation

Group and treatment	Tissue	UQ (μgm./gm.)	Vitamin A (I.U./gm.)	Liver peroxidation* (*E* at 520 mμ)
Control	heart	208		
	liver	106	116	14
0·05 per cent DPPD	heart	186		
	liver	96	173	8*
0·10 per cent 'Santoquin'	heart	227		
	liver	114	146	11*

*Significantly different from controls ($P = 0·01$).

Dietary selenium did not prevent lipid peroxidation in the rat, whether animals were fed casein-based vitamin E-deficient diets or 'necrogenic' vitamin E/selenium-deficient diets. In a typical experiment, groups of 16 weanling rats were fed a 'necrogenic' bakers' yeast diet, one group being supplemented with 0·05 p.p.m., another with 0·5 p.p.m. of selenium (as sodium selenite), and another with 0·01 per cent *dl*-α-tocopheryl acetate. Three rats in the control group died of liver necrosis at the twenty-third, twenty-sixth and twenty-ninth day; selenium or tocopherol fully protected the other animals. Livers were examined at 20 and 26 days for *in vivo* and *in vitro* peroxidation and the results show (Table 3) that, in contrast to tocopherol, selenium had no significant protective effect on peroxide formation in rat liver.

Table 3. Effect of Selenium on Lipid Peroxidation of Rat Liver

Group and treatment	Liver peroxides (*E* at 520 mμ) *in vivo*	*in vitro*
Control	6 (4–6)	9 (8–11)*
+ 0·05 p.p.m. selenium	6 (4–8)	10 (8–14)*
+ 0·5 p.p.m. selenium	6 (4–6)	11 (8–11)*
+ 0·01 per cent α-tocopheryl acetate	4, 4, 4	7, 6, 7†

* Mean and range of 7 determinations. † Individual determinations.

These experiments suggest that the mechanism(s) by which α-tocopherol and selenium increase ubiquinone in the rat can be divorced from the general anti-oxidant function of the former substance. Under conditions in which two powerful anti-oxidants have been demonstrated to carry out their function, they were unable to influence ubiquinone; selenium, on the other hand, had no demonstrable anti-oxidant properties, but a tocopherol-like effect on ubiquinone. This work will be reported in full elsewhere.

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Role of Selenium in Relation to Ubiquinone in the Rat

In a preliminary communication[1] and in more detailed work[2], we have shown that α-tocopherol and selenium independently control ubiquinone-levels in the rat, and a similar relation between tocopherol and ubiquinone has been found in the rabbit[3]. We have proposed a theory of vitamin E function which can be briefly summarized as follows. Although animal species vary considerably in their requirements for tocopherol, an even more important variation exists in individual tissue requirements for the vitamin, and in the rates at which tissues become depleted in vitamin E deficiency. Thus, in the rat, uterus normally contains a relatively high concentration of tocopherol and is rapidly depleted, whereas, in the rabbit, skeletal muscle is the tissue most readily depleted. In both these tissues, diminished ubiquinone-levels are the result and may be causally related to the specific syndromes of vitamin E-deficiency, fœtal resorption in the rat and muscular dystrophy in the rabbit. The remarkable species differences in vitamin E deficiency are, according to this hypothesis, a reflexion of local tissue tocopherol deficiencies.

We have now studied the implications of such a hypothesis with respect to the role of selenium. Selenium prevents or cures some symptoms of vitamin

Table 1. Effect of Orally Administered Selenium and α-Tocopherol (α-Toc.) on Ubiquinone (UQ) in Female Rats

Group and treatment	Heart UQ (μgm./gm.)	Heart α-Toc. (μgm./gm.)	Ovary UQ (μgm./gm.)	Ovary α-Toc. (μgm./gm.)	Uterus UQ (μgm./gm.)	Uterus α-Toc. (μgm./gm.)
Control	30	0·5	48	18	33	0·8
+ 40 μgm. selenium	58	1·1	76	16·8	36	2·4
+ 10 mgm. tocopheryl acetate	132	4·5	88	61·0	50	6·9

Table 2. Effect of Dietary Selenium and α-Tocopherol on Ubiquinone (UQ) in Female Rats

Group and treatment	Heart UQ (μgm./gm.)	Liver UQ (μgm./gm.)	Kidney UQ (μgm./gm.)	Uterus UQ (μgm./gm.)
Control	144	62	56	13
+ 0·1 p.p.m. selenium	195	93	66	12
+ 0·01 per cent α-tocopheryl acetate	170	92	70	22

E deficiency, its effect varying from species to species. Some syndromes, such as hepatic necrosis in the rat[4] and exudative diathesis in the chick[5], are prevented by either selenium or tocopherol. Other syndromes, such as gestation-resorption in the rat, are only preventable with tocopherol[6]; yet a third group of syndromes, such as muscular degeneration in lambs[7], may well be primarily selenium-deficiencies, only partially responsive to tocopherol. These differences must be explained if an understanding of the role of either compound is to be reached.

In a typical experiment, three groups of 8 female rats (3½ months old) were fed a 'necrogenic' fat-free yeast/sucrose diet designed to reduce tocopherol, selenium and ubiquinone in the animals' tissues to very low amounts. Rats in one group were dosed with 20 μgm. of selenium (as selenite) 48 and 24 hr. before death, and a second group with 5 mgm. of *dl*-α-tocopheryl acetate at the same times. The three groups were killed together. Hearts, uteri and ovaries were analysed by methods already described[8] (Table 1). Tocopherol-levels in heart and uterus were almost too low to measure; but the ovaries contained much tocopherol—being, with adrenals, the last tissue in the body to retain stores of tocopherol[2]. The ubiquinone concentration in deficient heart was very low, but was increased to high levels with α-tocopherol. Selenium had a similar effect (but less marked, due to the smallness of the dose). Selenium and tocopherol both markedly increased ubiquinone in the ovaries, but in uterus, although tocopherol was fully active in increasing ubiquinone, selenium was without effect. In another experiment groups of 6 female rats were reared for 10–12 weeks on a vitamin E-deficient diet. One group received a dietary supplement of 0·01 per cent *dl*-α-tocopheryl acetate, a second a supplement of 0·1 p.p.m. of selenium (as selenite), while a third group acted as controls. Both selenium and tocopherol increased ubiquinone in heart, kidney and liver; only tocopherol had an effect in uterus (Table 2).

While the reason for the failure of selenium to influence ubiquinone in the rat uterus but not in the ovary, which have a common blood supply, is unknown, it is not suggested that this is directly the reason for its failure to prevent foetal resorption in the rat; nor do we believe that ubiquinone enhancement in uterus by tocopherol explains the latter's action in preventing resorption. Rather, we regard the ubiquinone effect as diagnostic evidence of the ability or otherwise of these two substances to reach the embryos, where ubiquinone synthesis at a certain stage might be extremely critical. This work will be reported in full elsewhere.

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Tocopherol, Ubiquinones and Ubichromenols in Yeasts and Mushrooms

During work on vitamin E, we have been interested in obtaining animal diets rigorously freed of tocopherol. Methods of analysis now available[1,2] allow amounts of tocopherol much less than 1 μgm./gm. of diet to be determined and have already shown that many constituents of 'vitamin E-free' diets in fact contain appreciable amounts of tocopherol. Of particular interest is yeast, which has usually been held to be devoid of tocopherol (for example, Forbes and György[3]). When several kinds of commercial dried bakers' yeast were analysed by the above methods they were found to contain small quantities of α-tocopherol (of the order of 0·3 μgm./gm.) Eventually, fresh compressed bakers' yeast (Distillers Co., Ltd., 3 kgm.) was lysed by a method[4] using diethylamine as catalyst, and the solid residue was extracted with hot ethyl acetate. The extract was purified and analysed[1] for α-tocopherol, ubiquinone-30 and ubichromenol-30. In Table 1 the results are compared with those found on a replicate batch of yeast autolysed with ethyl acetate and extracted with hot benzene–alcohol (a method[5] used for ergosterol). It would appear that the former method is superior to the latter. The ubichromenol-30 was identified by comparing it with a synthetic specimen, prepared from ubiquinone-30 by Links's method[6]. Certain batches of yeast appeared to contain ubiquinone-35 instead of ubiquinone-30. The identity of the α-tocopherol was confirmed by isolating it chromatographically. The substance was strongly reducing, ran identically with α-tocopherol in two chromatographic systems, had an ultra-violet maximum at 291 mμ and an infra-red spectrum consistent with it being α-tocopherol.

Since it appeared possible that the tocopherol might have been of exogenous origin, samples of beet and cane molasses (the main organic constituents used for the commercial production of this yeast) were examined. Several hundred grams of each, dissolved

Table 1. Tocopherol, Ubiquinone and Ubichromenol in Yeast, etc.

Material	Ubiquinone (μgm./gm.)	Ubichromenol (μgm./gm.)	α-Tocopherol (μgm./gm.)
Dried baker's yeast (D.C.L.)	1·1	0·2	0·3
Compressed yeast (D.C.L.)			
(*a*) Diethylamine-treated	2·9	5·2	0·8
(*b*) Ethyl acetate-treated	0·2	0·5	0·2
Cane molasses	Trace	None found	0·2
Compressed bakers' yeast, laboratory grown	32·9	None found	0·8
Dried *Torula* yeast (American, type *B*)	341	420	2·5
Dried *Torula* yeast (American, type 361)*	137	349	4·2
Dried *Torula* yeast (British)	50	65	Trace
P. campestris (cap)	4·7	0·5	1·1
(gills)	7·2	0·4	1·2

* A special yeast produced for high content of vitamin B. D.C.L., Distillers Co., Ltd.

in water, were extracted in a continuous extractor with ethyl acetate. Analysis of the extracts showed that cane molasses did in fact contain a little α-tocopherol (Table 1), but beet molasses did not. In order to arrive at an unequivocal answer to the problem of the origin of yeast tocopherol, a culture of the commercial yeast was grown in the laboratory on a medium in which the only energy source was pure sucrose. Analysis of the compressed cake (300 gm.), lysed with diethylamine as before, confirmed the presence of α-tocopherol (identified as previously). Considerably more ubiquinone than in the commercial sample was also found, the increase probably being due to the more efficient aeration used in the laboratory, as found by Sugimura and Rudney[7].

Torula yeast (*Torula utilis*) has also been widely used as a constituent of vitamin E-free diets. Two commercial samples of dried *Torula* yeast (Lake States Yeast Corp.) were examined. They both contained considerable α-tocopherol, and were remarkable because of their large ubiquinone and, in particular, ubichromenol contents (Table 1). Yeast is the first natural substance we have so far encountered in which the concentration of ubiquinone is exceeded by that of ubichromenol. The latter is clearly the unidentified tocopherol-like substance previously reported in yeast by Cowlishaw and Prange[8]. Paper chromatographic separation of the *Torula* extracts revealed 3 ubiquinones and 3 ubichromenols. The former consisted mainly of ubiquinones-45 and -35, as already described[9], with a trace of ubiquinone-30. The three ubichromenols were isomeric with the quinones. All six substances were compared chromatographically with authentic samples, followed by individual isolation and determination of their ultra-violet spectra. A sample of British *Torula* yeast was examined (Table 1) and found to contain considerably less of the lipid constituents. However, this yeast also contained more ubichromenol than ubiquinone.

The common mushroom (*P. campestris*) contained amounts of ubiquinone, ubichromenol and α-tocopherol very similar to those in bakers' yeast (Table 1). It seems, therefore that, although in a previous survey[10] it was suggested that the synthesis of α-tocopherol might be limited to chlorophyll-containing organisms, this view can no longer be held.

We wish to thank the Lake States Yeast Corp., Rhinelander, Wisconsin, for their generosity both in providing specimens of *Torula* yeast and their useful information; also Distillers Co., Ltd., for kindly giving us samples of their cane and beet molasses. We also thank S. A. Price and L. Gare of these Laboratories, who provided us with yeast grown on a defined medium.

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An Unidentified Ubichromenol-like Lipid Constituent of Bakers' Yeast

During investigations of the unsaponifiable fraction of bakers' yeast (Distillers Co., Ltd.) by two-dimensional chromatography[1], a heavy spot was observed on the papers in a position very close to that expected for ubichromenol-30, which substance is present only in very small amounts in this yeast (preceding communication). The new substance was —like ubichromenol-30—slowly reducing to ferric chloride–dipyridyl; but, on papers pretreated with zinc carbonate containing a trace of sodium fluorescein[2] is weakly fluorescent under ultra-violet light, whereas the ubichromenol is observed as a quenching spot under the same conditions. By a combination of adsorption and reverse-phase partition paper chromatography, a few milligrams of the substance were obtained in a reasonable state of purity. Long runs in two reverse phase paper systems (*a*) liquid paraffin/95 per cent ethanol, and (*b*) olive oil/95 per cent ethanol, clearly distinguished the new substance from ubichromenol-30; the R_F values for these two substances in the latter system were 0·64 and 0·46, respectively. The new substance had absorption maxima at 255 and 282 mμ, with minima at 267 and 315 mμ (in ethanol). In the presence of dilute ethanolic alkali, the 282-mμ peak disappeared and a new peak at 345 mμ appeared. Well-defined isosbestic points occurred at 271 mμ and 322 mμ. These changes are similar to those described[2] for ubichromenol-50, with some displacement of the points, and probably indicate the presence of a phenolic OH grouping as in the latter. The infra-red spectrum had bands at ν 2,899, 2,809, 1,455, 1,373, 1,261, 1,208 and 1,059 cm.$^{-1}$, similar to those found in a specimen of ubichromenol-50 (kindly given by Prof. R. A. Morton). Substance 282 (so-called because the single peak at 282 mμ characteristically distinguishes it from the ubichromenols) was chromatographically distinct from the fluorescent substance, 3-formylindole, which is present in certain animal tissues[4] and has $\lambda_{max.}$ 282 (in cyclohexane) and $\lambda_{max.}$ 294 (in ethanol). Substance 282 was found to be strongly active, like α-tocopherol, in the *in vitro* erythrocyte haemolysis test.

Forbes and György[3] have already isolated from bakers' yeast a blue fluorescent substance, which has

some vitamin E-like activity and is also strongly active in the hæmolysis test. This substance has been identified[6] as 2-(6-hydroxy-2-methoxy-3,4-methylenedioxyphenyl)-benzofuran and is clearly distinguishable from substance 282 on chromatographic and spectral evidence. In fact, these are not the only two fluorescent substances in the non-saponifiable fraction of bakers' yeast: yet a third non-reducing substance, strongly fluorescent, is present and has chromatographic properties almost identical with those of α-tocopherol.

It is interesting that substance 282 occurs in bakers' yeast and also in the mushroom (*P. campestris*), both of which contain very little ubichromenol. *Torula* yeast, on the other hand, which contains much ubichromenol (preceding communication), contains no detectable substance 282.

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Electrophoretic Behaviour of Rat Serum Amylase

Determinations of the electrophoretic behaviour of human serum amylase[1] showed that the largest amount of amylase migrated with the albumin fraction and that a significant amount also migrated with the γ-globulins. Our preliminary observations[2] indicated that this was not the case for rat serum. The Dolcourts[3] found that this was also not true for mouse serum, where about 75 per cent of the total serum amylase migrated with β_1- and β_2-globulins.

Sera were obtained from both normal rats and those suffering severe liver damage from treatment with N-nitrosodimethylamine[2,4]. The proteins of these sera were separated by paper electrophoresis with a Spinco paper electrophoresis apparatus, Model *R*, using a new filter paper, Schleicher and Schuell 2043.4 *gl*, thinner than the Whatman paper previously used[1]. The protein fractions were eluted with 0·9 per cent sodium chloride and analysed for amylase by a micro modification[1] of Van Loon's amyloclastic method[5].

As indicated in Table 1, the largest fraction of the serum amylase recovered was that associated with the β-globulin (70 per cent) and a lesser amount (about 25 per cent) with the γ-globulins, a pattern somewhat similar to that found for mouse serum[3]. The leading fractions contained amounts so small as to be almost insignificant. With sera from rats with liver damage, the amylase in the β- and γ-globulin fractions was reduced to less than 30 per cent of that in the normal sera, while the very small amounts in the albumin and α-globulin fractions remained essentially the same as in the normal.

Table 1. Distribution of Amylase in Rat Serum

Serum fraction	Amylase units/100 ml. serum	
	Normal*	N-nitrosodimethylamine* treated
Albumin	24	35
α_1-Globulin	19	19
α_2-Globulin	31	26
β-Globulin	1,012	287
γ-Globulin	337	93
Total of all fractions	1,443	460

* Five animals in each group. Duplicate determinations on each animal.

The fact that liver damage leads to marked reduction in the amylase of the β- and γ-globulin fractions might be interpreted as indicative that the amylase normally found in these fractions is produced in the liver. Because of the uncertainties in the interpretation of measurements of paper electrophoresis caused by protein–protein and protein–paper interactions, we would be cautious about making this interpretation unequivocally from these data alone. However, this interpretation would strengthen our previous conclusion from other data[2,6,7] that the liver is a source of amylase production.

Whatever the conclusions concerning the relationship of the liver to serum amylase, we wish to point out that the distribution pattern of serum amylase may vary from one species to another. That for the rat is definitely different from that for man.

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Identification of 3,4,5-Trimethoxyphenylacetic Acid as the Major Metabolite of Mescaline in the Dog

Mescaline (3,4,5-trimethoxyphenylethylamine), an alkaloid obtained from *Anhalonium lewinii* and *Trichocereus terscheckii*, has been the subject of many investigations. After oral administration of mescaline to dogs, Slotta and Müller[1] were able to isolate 38 per cent of the mescaline as 3,4,5-trimethoxyphenylacetic acid but were unable to detect any of the parent compound in the 24-hr. urine. These results could not be confirmed by Cochin and co-workers[2], who reported that only 'trace' quantities of 3,4,5-trimethoxyphenylacetic acid were excreted in this species, but that 28–46 per cent of a dose, administered parenterally or orally, was excreted as the parent compound. Others[3–6] have reported similar findings of unchanged mescaline in the urine of human beings receiving the drug. The metabolism of this drug was re-investigated in the dog employing 8-^{14}C mescaline.

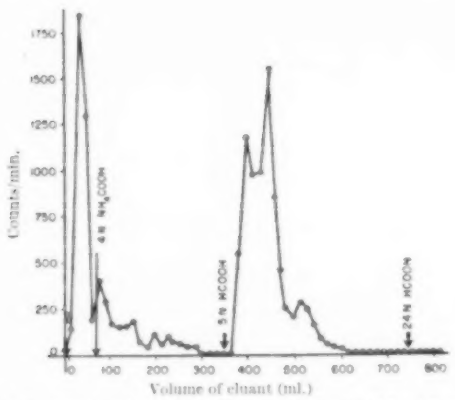

Fig. 1. Fractionation of acidified urine on 'Dowex-1' formate resin

Labelled mescaline (15 μc.) in a dose of 20 mgm./kgm. was administered intraperitoneally to mongrel female dogs anæsthetized with pentobarbitone sodium (35–40 mgm./kgm.). Urine was collected via an indwelling Foley catheter. Aliquots of urine (0·1–1·0 ml.) were combusted and assayed for radioactivity in a 250-ml. ionization chamber (Nuclear-Chicago model 6000). Excretion of radioactivity was determined for periods up to 13 hr. following administration of labelled mescaline. The values for radioactivity excreted during these experiments range from 55 to 62 per cent. Peak urinary excretion of radioactivity occurred within 2 hr. after administration of the drug.

Fractionation of acidified urine (*p*H 2–3) on 'Dowex-1' formate resin revealed the presence of two major peaks of activity (Fig. 1). The first peak of radioactivity when re-chromatogrammed on Whatman No. 52 paper (solvent system: water/acetic acid/butanol, 4 : 1 : 4) demonstrated an R_F value of 0·71–0·74, whereas mescaline had an R_F of 0·72 when chromatogrammed under similar conditions. The second peak of radioactivity, representing approximately 60 per cent of the excreted radioactivity, was eluted from the resin column with 5 *N* formic acid and had an R_F value of 0·91–0·92 when examined by paper chromatography.

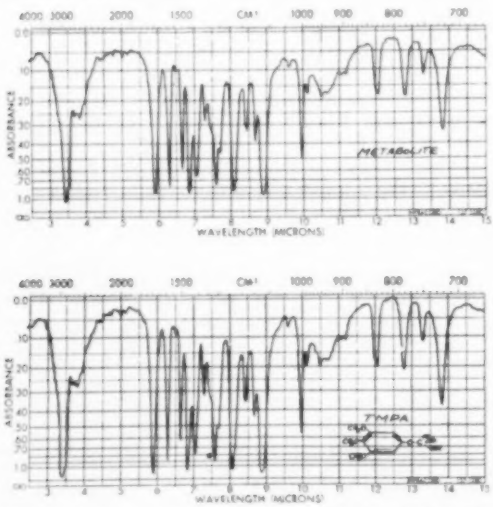

Fig. 2. Infra-red spectra of trimethoxyphenylacetic acid and metabolite of mescaline isolated from the urine of the dog

Acidified, unfractionated urine, or material corresponding to the second peak of resin-fractionated urine, was extracted with chloroform and/or diethyl ether. After evaporation of the latter solvent, the residue was washed with petroleum ether ('Skellysolve *B*') and then sublimed under vacuum. White crystalline material, melting point 118–119·5° C., was obtained. A mixed melting point with authentic 3,4,5-trimethoxyphenylacetic acid (melting point 118·5° C.) showed no depression. The infra-red absorption spectra of the metabolite and authentic 3,4,5-trimethoxyphenylacetic acid were identical (Fig. 2). Elemental analysis of the metabolite revealed the following values: found: C, 57·51; H, 6·10; N, 0·0; O (by difference), 36·39; calculated: C, 58·40; H, 6·20; N, 0·0; O, 35·40.

These results clearly indicate that deamination with resultant formation of a carboxylic acid is the major pathway of metabolism of mescaline in the dog, but that a significant amount of unchanged drug is also excreted in this species.

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Method of dissolving Triacetyl-oleandomycin for the Assay of Sensitivity of Micro-organisms

The usual *in vitro* tests of the sensitivity of bacteria to antibiotics are not applicable to triacetyl-oleandomycin (TAO), known in Great Britain as 'Evramycin' and in the United States as 'Cyclamycin', since it is almost insoluble in water. In spite of this, TAO is known to be clinically effective, and after oral administration it attains a high concentration in the blood.

It seems that in order to enter the blood-stream and to reach the peak-concentration in as short a time as about 2 hr., this antibiotic must be converted into an absorbable form very soon after ingestion, either in the stomach or in the upper segment of the intestine.

My experiments *in vitro* showed that TAO is insoluble in the duodenal juice, but it dissolves readily in the gastric secretion, samples of filtered, unfiltered and also of boiled gastric juice being equally effective solvents. This suggests that gastric hydrochloric acid is the effective substance.

TAO dissolves readily in $N/10$ hydrochloric acid (a concentration corresponding to that found in normal gastric juice), but neither gastric juice nor $N/10$ hydrochloric acid could be used as solvents of TAO for assays of sensitivity, since these reagents alone produce narrow zones of inhibition of bacterial growth and may cause considerable alteration and discoloration of complex media.

A series of tests with a wide range of hydrochloric acid concentrations showed that $N/100$ hydrochloric acid had no effect on media or micro-organisms, and dissolved TAO satisfactorily. To provide a margin of safety, however, $N/200$ hydrochloric acid is recommended as the solvent for TAO in sensitivity assays.

Triacetyl-oleandomycin requires an acid medium for its solubilization, and because of this one may speculate whether the speed of absorption and effectiveness of this antibiotic could be increased by dissolving it beforehand or supplementing it with dilute hydrochloric acid during its oral administration, especially in patients with achlorhydria or hypochlorhydria.

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Crystalline α-Kojibiose

Kojibiose (2-O-α-D-glucopyranosyl-D-glycopyranose) was first detected in saké and its moromi[1], and it was isolated from hydrol[2], koji extract[3] and honey[4] as its crystalline α- and β-octaacetates. Chemical synthesis[5,6] of this sugar was also achieved. But the crystallization of free sugar was hitherto unsuccessful, so its properties such as melting point, specific rotation or its form of crystal were still unknown. We have now succeeded in crystallizing kojibiose and examining its properties.

The same method as reported previously[7] was used for preparation of the kojibiose; but in this work the culture medium of *Leuconostoc mesenteroides* contained sucrose (9 per cent) and lactose (15 per cent) instead of sucrose (2 per cent) and lactose (10 per cent), and then a branched trisaccharide (O-β-D-galactopyranosyl-(1 → 4)-O-[α-D-glucopyranosyl-(1 → 2)]-D-glucopyranose) and lactosucrose[8,9] (O-β-D-galactopyranosyl-(1 → 4)-O-α-D-glucopyranosyl-(1 → 2)-D-β-fructofranoside) were obtained together. After removal of most of the lactose and dextran by addition of an equal volume of ethanol, the supernatant was concentrated and fractionated by carbon column chromatography. 95 gm. of lactosucrose and 140 gm. of the branched trisaccharide contaminated with a small amount of lactosucrose were obtained from 15 litres of the culture medium. The contaminated lactosucrose in the branched trisaccharide fraction was hydrolysed to lactose and fructose with 0·5 N sulphuric acid at 60° C. for 30 min. and was removed by carbon column chromatography. 97 gm. of the branched trisaccharide was obtained. 10 gm. of the lactase preparation of *Saccharomyces fragilis* (kindly supplied by Dr. Henry Roberts) and 90 gm. of the above branched trisaccharide were incubated in 1 litre of phosphate buffer (*p*H 6·2), and 48 gm. of amorphous kojibiose was obtained by carbon column chromatography.

This crude kojibiose was dissolved in 200 ml. of hot methanol, and the solution was refluxed gently, followed by filtration of the insolubles on 'Celite', and was left to cool at room temperature and then

Fig. 1

the kojibiose crystallized. 30·5 gm. of crystalline free sugar was obtained. Recrystallization was carried out by dissolving 10 gm. of the above crystals in 15 ml. of hot water and adding 35 ml. of methanol after being decolorized with charcoal. The crystals obtained took the form of fine prisms (Fig. 1). On drying in vacuum at 100° C. for 2 hr. over phosphorus pentoxide, crystalline kojibiose, which was somewhat hygroscopic, showed a melting point of 187–88° C. (uncorrected) and $[\alpha]_D^{18} = +162° \rightarrow 137°$ (17 hr.) (c., 2·1 in water) (calculated for $C_{12}H_{22}O_{11}$: C, 42·11; H, 6·48 per cent; found: C, 42·22; H, 6·48 per cent). The downward mutarotation showed that this crystalline kojibiose was α-isomer. This fact was further confirmed by formation of its acetyl derivative. Namely, only α-kojibiose octaacetate (m.p. 166° C.) was obtained when the acetylation was carried out at a low temperature by using pyridine as catalyst, while both α-kojibiose octaacetate (m.p. 166° C.) and β-kojibiose octaacetate (m.p. 117° C.) were obtained by the usual method using sodium acetate. Neither acetate showed depression of melting point on admixture with the authentic samples synthesized chemically by Matsuda[5].

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PHYSIOLOGY

Plastic Changes of Spinal Monosynaptic Responses from Tenotomized Muscles in Cats

In an attempt to reduce muscle afferent activity, the tendons of some hind-limb muscles of cats were cut. It was postulated that this would prevent the development of effective tension, reduce passive stretching, and so induce relative disuse of the central synaptic connexions of the muscle afferent nerves.

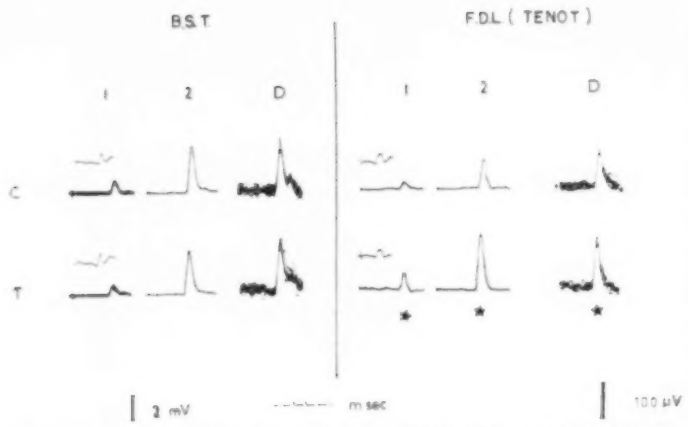

Fig. 1. All reflexes in this figure were taken from one typical experiment. Columns 1 and 2, respectively, are monosynaptic reflex responses for each nerve recorded from *L7* ventral roots before and after tetanic conditioning at 400 c./sec. for 10 sec. The afferent volleys from the cord dorsum are inset. *C*, Control side; *T*, tenotomized side. Biceps-semitendinosus nerve (*B.S.T.*) provided a bilateral control. Flexor digitorum longus (*F.D.L.*) was tenotomized. Dorsal spinocerebellar tract responses occupy columns *D*. Stars indicate enhanced responses from tenotomized muscle

At initial aseptic operations of 23 cats (inset Fig. 2) tenotomy was performed by excising about 10 mm. of the tendons of the following muscles on one side: triceps surae, flexor digitorum longus, and flexor hallucis longus. A dummy operation was made on the contralateral side.

One to four weeks after tenotomy, the spinal monosynaptic reflex responses were tested by two methods during the final acute experiments under pentobarbitone anaesthesia.

(1) The skin of both hind-limbs and the back was formed into pools which were filled with warmed paraffin oil. The cut nerves from the tenotomized and also from the control muscles (biceps-semitendinosus, quadriceps femoris, and peroneal group) in both hind-limbs were stimulated electrically. The reflex responses were recorded monophasically from the central cut ends of ventral roots *S1*, *L7*, *L6*. Further details of methods are the same as those given in a previous communication[1].

(2) Monosynaptic responses in the dorsal and ventral spinocerebellar tracts were also recorded[2]. The dorsal funiculi were dissected off the spinal cord between *T12* and *L2*, and the remaining portion of the cord was then hemisected longitudinally[3]. Dorsal spinocerebellar tract responses to both group *1a* and *1b* afferent volleys were recorded from the ipsilateral half-cord[3], while the ventral spinocerebellar tract reflexes from only group *1b* afferents were recorded in the contralateral half-cord[4].

In Fig. 1 the typical monosynaptic reflexes recorded monophasically from ventral roots show the symmetry of control reflexes evoked by biceps-semitendinosus volleys into both ventral roots. By contrast reflexes evoked from the nerve to flexor digitorum longus muscle are, significantly, 50–100 per cent larger from the nerve to the tenotomized muscle (Fig. 1). Though the conduction velocities for the afferent volleys (inset) were equal, a slight shortening of the central latency (mean about 0·1 msec.) was observed in reflex responses evoked from nerves to tenotomized muscles. The results described for biceps-semitendinosus and flexor digitorum longus were duplicated by the other muscles tested. Fig. 2 gives further details. These results are in close agreement with those obtained by Beranék and Hnik[5], who used similar techniques.

Spinocerebellar tract responses evoked by biceps-semitendinosus and flexor digitorum longus volleys in the same experiment (Fig. 1) illustrate the pooled results shown in Fig. 2. There is symmetry of the control dorsal spinocerebellar tract responses from hamstring, peroneal, deep tibial nerves, and of the ipsilateral ascending mass discharges from a skin nerve, sural. The nerves to tenotomized muscles, however, show a 45–55 per cent enhancement of their dorsal spinocerebellar tract responses with no significant change in ventral spinocerebellar tract responses.

Since the dorsal spinocerebellar tract responses arise more from group 1*a* than 1*b* muscle afferent fibres and since ventral spinocerebellar tract has exclusively 1*b*

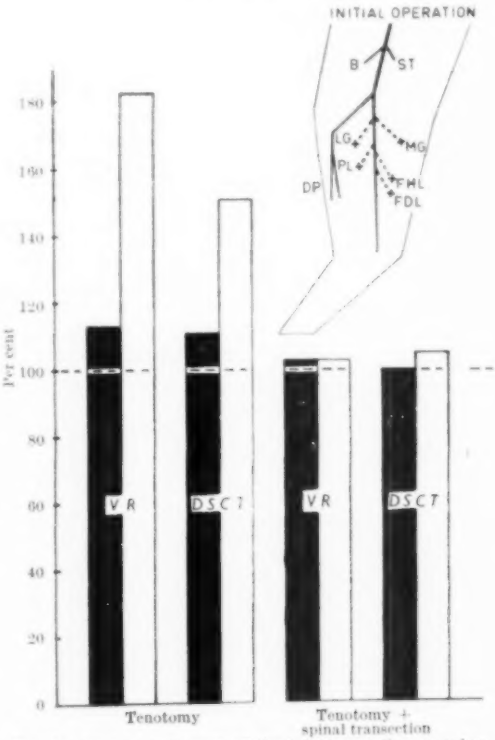

Fig. 2. Inset is a diagram of the initial operative procedure showing the nerves to tenotomized (+ - - -) and normal (——) muscles. Monosynaptic responses recorded from ventral roots *VR* and dorsal spinocerebellar tract response *DSCT* from ipsilateral half-cord. The results depicted in the histogram are averages of pooled reflex responses from 21 animals in the first group and 8 in the second group. The ordinate indicates the mean percentage ratio of corresponding reflexes from tenotomized side/normal side for the groups of nerves to normal (filled columns) and tenotomized (open columns) muscles. Thus 100 per cent indicates bilateral symmetry and a ratio of 1·00. The mean enhancement of *VR* and *DSCT* responses from tenotomized muscle is statistically significant, $P < 0.01$, and is prevented by spinal transection with tenotomy

connexions, our results suggest that the group Ia muscle afferents from the muscle spindle are responsible for the enhancement of dorsal spinocerebellar tract monosynaptic reflex responses, which thus parallels the increased monosynaptic reflexes in ventral roots.

Comparison of muscle wet weight in both hind-limbs of all cats revealed that all muscle groups in the tenotomized leg wasted to some extent. The amount of wasting of tenotomized muscles themselves was much greater and persisted over several weeks, while control muscles on the tenotomized side began to recover their small weight losses after 9–10 days.

Since little is known of proprioceptor function in tenotomized muscles, preliminary attempts were made (in 40 muscles from 10 cats) to analyse the afferent activity from chronically tenotomized muscles by recording directly from the distal segment of cut muscle nerves. A significant 25–40 per cent increase was observed in spontaneous afferent spike discharges from chronically tenotomized muscles.

In further experiments transection of the spinal cord at T10–11 level immediately prior to tenotomy prevented, over the same period of survival, the development of both the reflex enhancements (Fig. 2), and the increased afferent discharges induced by tenotomy alone. This effect of cord section, which abolishes supraspinal gamma efferent activation, suggests that an over-active gamma loop mechanism could be responsible for the increased spindle discharges, which could lead to reflex enhancements.

We conclude from available evidence that tenotomy of muscle results in increase of the monosynaptic responses evoked by group Ia afferent volleys. There is some evidence suggesting that this effect is brought about by increased discharges of Ia impulses from the chronically tenotomized muscles, that is, that it is due to increased synaptic use. The effects are prevented by spinal cord-section (T10–11) at the time of tenotomy.

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Role of Biliary Alkaline Phosphatase in the Guinea Pig

Although the part played by intestinal alkaline phosphatase in digestion and absorption is still not clear, it has long been postulated that the high concentration in the duodenum and intestine is concerned with the absorption of glucose[1]. Following adrenalectomy, Verzar *et al.*[2,3] showed that intestinal alkaline phosphatase was reduced and glucose absorption decreased. Administration of adrenal cortical hormones caused regeneration of the phosphatase.

Alkaline phosphatase is known to be secreted in the bile of mammals and it has been suggested that the biliary enzyme plays some part in digestion[4]. The present experiments were designed to see if there were any relation between biliary and intestinal alkaline phosphatase, in particular to see if the high concentration in the intestine were a result of the adsorption of biliary phosphatase by the mucosa. Such a system might be advantageous in replacing enzyme lost either by a mechanical rubbing off or by attack by digestive enzymes.

Duodenal alkaline phosphatase was therefore compared in normal guinea pigs and in guinea pigs in which the common bile duct had been tied and a gall bladder fistula made. In previous reports of guinea pigs with biliary fistulæ, the animals died within 24 hr.[4]. It was found that operated animals drank very little for the first 48 hr., and, as the daily output of bile from a fistula could reach 150–200 ml. (cf. 500 ml. for an adult man), a control of the fluid balance was planned in an attempt to increase survival times. In practice fluid was injected either subcutaneously or intraperitoneally. The fluid injected was Krebs's physiological saline containing vitamins C and K. In the absence of vitamin K, local haemorrhages occurred.

Male guinea pigs were given vitamin K (0·1 mgm. 'Synkayvit') and vitamin C (10 mgm.) before their operation. The operation was carried out under nembutal and ether anæsthesia and at the beginning of the operation 20-ml. fluid was injected subcutaneously into the axilla. Immediately following the operation, 20-ml. fluid was injected intraperitoneally and a further 20 ml. given subcutaneously 1 hr. later. Thereafter injections of fluid were given at about 3-hr. intervals in an attempt to keep the body-weight constant. The flow of bile was considerably reduced after 48 hr. and it was found practical to maintain operated animals in a healthy condition for at least eight days.

A number of control and experimental animals were killed and duodenal samples rapidly removed. These were freeze-dried and embedded in paraffin wax *in vacuo*. After sectioning they were fixed in 90 per cent alcohol. The alkaline phosphatase of the brush border of the mucosal cells was estimated quantitatively by the method of Barter and Danielli[5]. Phosphatase activity was expressed in standard units of gm. phosphate hydrolysed per gm. of tissue per min. and the results obtained are shown in Table 1.

The results for operated animals show a consistently higher phosphatase activity compared with those from control animals which have not undergone operation. This result is opposite to that which would be expected if duodenal alkaline phosphatase was partly absorbed from the bile. The higher concentration found may indicate a reduced removal of duodenal phosphatase by mechanical or enzymic factors since the food intake of operated animals was lower than in the control animals. Alternatively, adrenal cortical hormones may have increased in the operated animals and caused the increase in duodenal phosphatase.

Table 1

Guinea pig	Period of biliary fistula (days)	Duodenal phosphatase in standard units			
		Proximal duodenum		Distal duodenum	
		Site 1	Site 2	Site 1	Site 2
1 (control)	—	0·050	0·048	0·09	0·064
2 (control)	—	0·063	0·072	0·032	0·062
3 (control)	—	0·064	0·075		
7	5½			0·29	0·52
				0·44	0·46
8	8	0·17	0·46	0·14	0·22
9	7	0·36	0·25	0·22	0·22
		0·49	0·27		
11	2			0·11	0·15
				0·11	0·17

I wish to thank Dr. R. S. Snell for his help with surgical procedures, Mr. C. H. O'Neill for his help in estimating alkaline phosphatases and Mr. A. T. Green and Mr. J. Storey for assistance. I am also grateful to Prof. J. F. Danielli, Dr. J. Stubbs and Dr. W. F. Widdas for helpful discussion.

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Alkaline Phosphatase in Cell Cultures of Human Origin

In an attempt to define some of the changes which cells undergo in adaptation to growth *in vitro*, work has been carried out on the metabolic and enzymatic activities of a variety of established cell cultures, mainly of human origin. For this work, cells were cultured in several media, including Eagle's medium[1] and *M*199[2] containing 10 or 15 per cent undialysed human serum, or in a nutrient medium described by Marcus *et al.*[3] containing 20 per cent undialysed human serum. Cells were grown for 6–8 days on glass surfaces at 37° C. in an atmosphere of 5 per cent carbon dioxide in air, and dispersed with 0·05 per cent trypsin in saline. They were collected by centrifugation at 500*g*, washed and resuspended in 0·25 *M* sucrose, and disrupted with a 10-kc./s. Raytheon sonic oscillator for 1–5 min. Cell protein was measured by the procedure of Lowry *et al.*[4].

The initial findings confirmed observations made by Lieberman and Ove[5] with regard to the similarity in specific activities of catalase, glucose-6-phosphate dehydrogenase, rhodanese and β-glucosidase among cell-free preparations of various cell lines. On the other hand, a striking dissimilarity was noted in alkaline phosphomonoesterase activity as measured by the hydrolysis of *p*-nitrophenylphosphate in 1 *M* 2-amino-2-methyl-1-propanol buffer, at *p*H 10·6, according to Lowry's technique[6].

Table 1 summarizes the specific activities for alkaline phosphatase in sonicates of a variety of established human cell lines, including the parental and three clonal strains of the *Z* liver line derived from an infant with congenital atresia of the bile ducts, and of a recently explanted bovine embryonic kidney cell line. As can be noted, alkaline phosphatase activity with sonicates of the Chang liver line[7] is two-fold greater than that of human intestine[8], three-fold greater than that of *KB* (Eagle)[9] and anywhere from 25- to 200-fold greater than that of other cell lines. After one or two successive single cell platings according to the technique of Puck *et al.*[10] several clonal strains of Chang liver have been obtained which show differences in alkaline phosphatase activity. Sonicates of one of these clonal strains, which can be defined by the gross morphological characteristic of a smaller cell size, have a specific activity which is only 1/40 that of the parental strain.

Table 1. ALKALINE PHOSPHATASE ACTIVITY OF MAMMALIAN CELLS IN CULTURE

Cell line	Activity, *p*H 10·6
Chang liver	21·88*
Intestine (Henle)	9·65*
KB (Eagle)	6·56
Z Liver-P.S.	0·53
Z Liver-1	0·15
Z Liver-2.4	0·14
Z Liver-4.4	0·84
HeLa-S3	0·12
HeLa-3213.4	0·22
MAF (Gray)	0·71
Bovine kidney	0·19

* Specific activity = μM *p*-nitrophenyl phosphate hydrolysed per mgm. protein in 30 min. at 38° C. in 1 *M* 2-amino-2-methyl-1-propanol – hydrochloric acid buffer, *p*H 10·6.

Separation of cell sonicates by differential centrifugation in 0·25 *M* sucrose[11] reveals the major portion of activity for all cell lines in the microsomal fraction. Extraction of a 10 per cent microsomal preparation with *n*-butanol[12] yields up to 9–10-fold purification of the phosphatase activity. Kinetic studies with the enzyme from the Chang liver microsomal fraction show the reaction to be zero order with the activity linearly dependent on enzyme concentration over a 100-fold range. The *p*H optimum is 10·6 with a decline to 10 per cent of maximal activity at *p*H 8·0. No activation with Mg^{2+} is found using *p*-nitrophenylphosphate as substrate, but inhibition is observed with Be^{2+}, Zn^{2+}, Mn^{2+}, CN^- and cysteine. Concentrations of 10^{-2} *M* inorganic phosphate are required for inhibition of activity. The enzyme exhibits a broad substrate specificity showing activity against *p*-nitrophenylphosphate, β-naphthylphosphate, β-glycerophosphate, adenosine monophosphate, glucose-6-phosphate and ethanolamine phosphate in decreasing order. Work is in progress to characterize further the physical-chemical properties of these enzyme preparations, some preliminary results of which indicate qualitative as well as quantitative differences in properties of enzymes derived from different cell lines.

During the course of this work, it was noted that the specific activity of alkaline phosphatase in Chang liver sonicates shows some variation over a four-fold

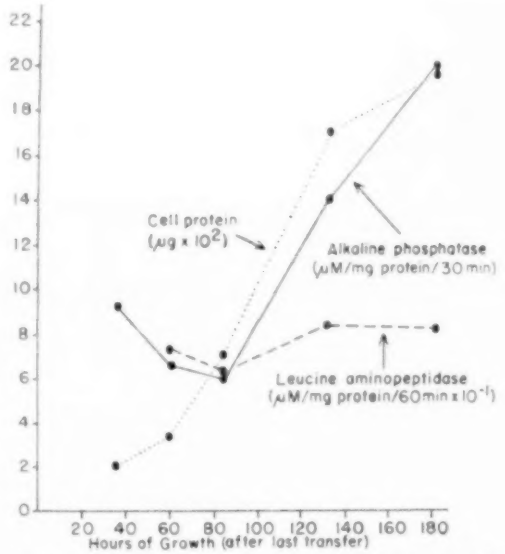

Fig. 1. Change in specific activity of alkaline phosphatase and leucine amino-peptidase in Chang liver sonicates with growth

range, although it is consistently higher than the activity of other cell lines. This variability can be correlated with the duration of growth following their last transfer, and in general, the longer the growth period the higher is the specific activity observed. These findings are illustrated in Fig. 1, where during a single growth-cycle of 180 hr., when cell protein increases ten-fold, the specific activity of leucine aminopeptidase remains constant but the specific activity of alkaline phosphatase rises to a value of 20·00 at 180 hr. of growth after falling from 9·50 initially to 6·00 at 84 hr.

Of interest are the recent observations of induced synthesis of alkaline phosphatase in *E. coli*[13,14], *B. subtilis*[15] and yeast[16] in response to removal of the repressor effect of inorganic phosphate in the growth medium. Preliminary work on inorganic phosphate concentrations in the nutrient medium reveal no alterations during the growth of Chang liver cells which can be correlated with the change of alkaline phosphatase activity. Work is now in progress to define more clearly whether an inducer or repressor mechanism plays some part in the differential activation or synthesis of alkaline phosphatase in these cells and whether such alterations, like those demonstrated by De Mars for glutamine synthetase[17], are characteristic of other enzyme systems.

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Prevention by Vagotomy of Erythrocytosis induced by Hypoxæmia

WHILE investigating the effect of fluid aspiration into the lungs[1], observations were made on erythrocytosis induced by hypoxæmia, which to our knowledge have not yet been described.

Sheep were anæsthetized with 'Thiopentone', intubated, and given 1–3 ml. kgm. fresh water into the trachea. Before and 5 min. following the latter procedure, blood samples were taken from the femoral artery through an indwelling cannula. Arterial oxygen saturation, haemoglobin and *p*H were determined and arterial oxygen tensions calculated. Observations carried out on 24 intact and 24 vagotomized sheep are reported here. Vagotomy was performed bilaterally on the neck prior to the control period.

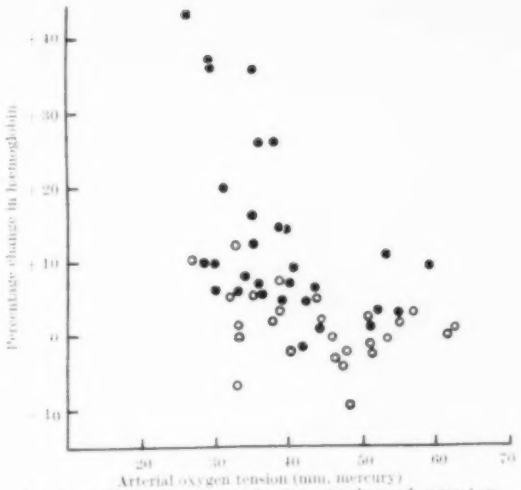

Fig. 1. Relationship of arterial oxygen tension and percentage change in haemoglobin content in intact (●) and vagotomized (○) sheep 5 min. following the induction of hypoxæmia. Each dot represents one animal. Oxygen tension is given in mm. mercury

Results are shown on Fig. 1. The arterial oxygen tension 5 min. following the inhalation of water was related to the percentage change in haemoglobin.

Water inhaled into the lungs is rapidly absorbed and remains unaffected by vagotomy[2]. Both groups were given strictly equal quantities of water; the resulting haemodilution is therefore comparable.

Erythrocytosis appears to commence rather abruptly at an arterial oxygen tension of about 35–40 mm. mercury. This is in good agreement with earlier observations, suggesting a critical oxygen tension of 40 per cent.

In experiments reported in the literature, hypoxæmia was caused by the inhalation of gas mixtures low in oxygen. Alveolar oxygen tension in our animals was invariably normal[1]. It seems justifiable to conclude that arterial unsaturation is in itself a sufficient stimulus to mobilize the stored red cells in the body.

A comparable degree of hypoxæmia failed to cause erythrocytosis in our vagotomized sheep ($r = -0{\cdot}153$; $P = 0{\cdot}40$). The nerves were divided well below the carotid sinus; its denervation could scarcely have been responsible for the absence of the reaction.

Splenic[3] and hepatic contraction, and an increase in splanchnic blood-flow, appear to be the accepted mechanism of hypoxic erythrocytosis. Splanchnic stimulation is followed by similar changes, while electric stimulation of the peripheral end of the divided vagus was without an effect. The profound fall in hæmatocrit during anæsthesia[4] and following the administration of chlorpromazine and dihydroergotamine[5] is accompanied by an increase in the red-blood cell content of the spleen.

Barcroft and Stephens[2] suggested that splenic contraction is the effect of hypoxaemia on the central nervous system. Our observations would therefore suggest that it is the absence of an afferent impulse which accounts for failure to observe hypoxic erythrocytosis after vagotomy.

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Relationship of the Sarcoplasmic Reticulum to Sarcolemma in Sheep Cardiac Muscle

Since Huxley and Taylor[1] demonstrated that in striated muscle each myofibril segment probably receives an individual stimulus to contract, electron microscope studies have suggested that the most likely pathway for such stimuli from the sarcolemma to the myofibrils is the sarcoplasmic reticulum[2], particularly[3] its transverse tubular elements (also named the 'transverse sarcotubular system'[4]). Theories about this have recently been elaborated and the evidence has been reviewed[5,6]. Such theories are necessarily based on the possibility that the membrane of the tubules is polarized and is capable of undergoing depolarization in the same way as the plasma membrane (inner layer of sarcolemma).

The question of continuity between plasma membrane and sarcoplasmic reticulum is a somewhat vexed one. Such continuity appears to occur in certain non-muscular cells[7,8], and it has been suggested or demonstrated also for both cardiac[2,9–11] and skeletal muscle[12,13]. This could not, however, be proved by serial sections in a major study of skeletal muscle[4], and the theories put forward[5,6] concerning impulse conduction by the sarcoplasmic reticulum are not based on a concept of communication between the lumen of the sarcoplasmic tubules and the extracellular fluid, although Huxley[14] favours such a concept on physiological grounds. Lindner[11] found that the transverse tubules in the dog myocardial cells had triple-layered membranes, like the sarcolemma, and he suggested that these tubules might be continuous with invaginations of the sarcolemma.

We have studied the fine structure of sheep cardiac muscle and we have found evidence of two types of tubular structure within the cell. One type is rather sparse in our material, possibly due to fixation artefact, and consists of delicate irregular small tubules, some of which are in contact (if not actual continuity) with the inner layer of the triple-layered sarcolemma (Fig. 1), in agreement with previously published work[5,9]. The other type is usually seen as cross-sections of tubules, lying between the myofibrils, usually opposite *Z* bands (Fig. 2). These tubules are comparatively large with triple-layered walls, identical in thickness and appearance to the sarcolemma.

Fig. 1. Electron microscope (Siemens Elmiskop 1) photograph of edge of sheep myocardial cell. Part of a network of fine tubules can be seen, apparently continuous with the plasma membrane (inner layer of sarcolemma). (× 45,000)

When the plane of section passes longitudinally between two myofibrils, the transverse tubules are cut longitudinally (Fig. 3), and the walls of some of the more superficial ones can be seen to be continuous with invaginations of the sarcolemma, as suggested by Lindner[11]. We feel that the electron micrographs cannot be satisfactorily interpreted in any other way: complete proof of the continuity of the whole transverse tubular system and the sarcolemma will depend on a three-dimensional picture built up from serial sections, but the present findings go far towards confirming Huxley's theories[1,14] of muscle activation.

This concept makes it much easier to accept the theory of a polarization of the sarcoplasmic reticulum, as it implies that this part of the sarcoplasmic reticulum is actually an integral part of the sarcolemma and necessarily undergoes the same electrical and chemical changes as the sarcolemma. The concept also implies that the lumen of this system of tubules is in communication with the extracellular space, and that the total area of sarcolemma (as Siekevitz[15] has suggested for other cells) is much greater than simply the external surface area of the cell. This may help to explain the great rapidity of the ionic fluxes which take place across the sarcolemma.

One may speculate further whether the alternate contraction and relaxation of the cell provide a pumping of extracellular fluid out of, and into, the system of tubules, and whether this might be of importance in the nutrition of the cell as well as in the electrical events of depolarization and repolarization.

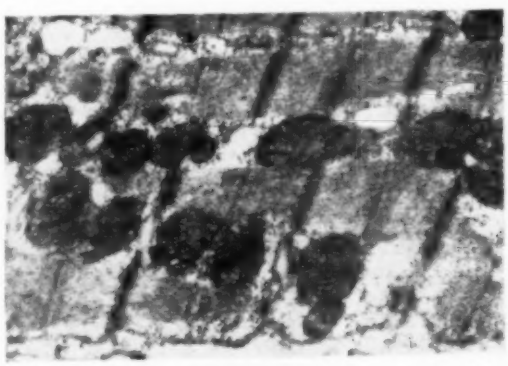

Fig. 2. Lower-power view, showing myofibrils, mitochondria, and cross-sections of the larger type of tubular structures with walls similar to the sarcolemma. (× 17,000)

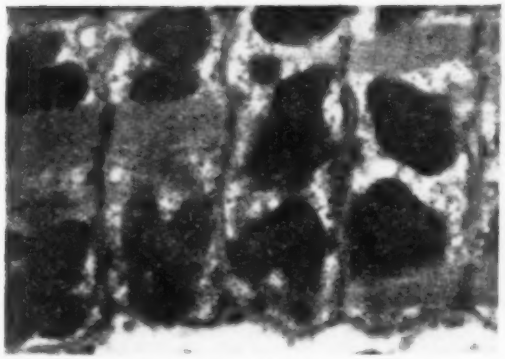

Fig. 3. Longitudinal section which has passed between two sub-sarcolemmal myofibrils. The walls of one of the longitudinally sectioned tubular elements are continuous with a sarcolemmal invagination, and the lumen communicates with the exterior. (× 12,000)

It is evident that this concept of myocardial cell structure will require a re-appraisal of the physiology of the myocardium and may help to solve some of the problems associated with the electro-chemical phenomena of the heart. It must be emphasized, however, that the present report is based on observations of cardiac muscle from the sheep only, and that the findings do not necessarily apply to voluntary muscle.

One of us (F. O. S.) is indebted to Dr. T. E. Lowe, director of the Baker Medical Research Institute, for suggesting this work, and to Dr. P. L. Bazeley, director of the Commonwealth Serum Laboratories, for access to electron microscope facilities.

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Partition of Calcium and Phosphorus Excretion in the Laying Hen

The need for surgery as a prerequisite to the separate collection of urine and faeces in birds has restricted our knowledge of their excretion pattern. Recently, the nitrogenous excretions of chickens have been investigated[1], but no data have as yet been published on the partition of calcium and phosphorus excretions. In order to study these excretions in laying hens, colostomies were performed by exteriorizing the distal end of the colon at a point between the ischium and the abdominal midline at the right side, approximately 1 in. anterior to the ventral lip of the cloaca, essentially as described by Ariyoshi[2]. In most birds the operation did not disturb egg production. For the collection of faeces, a polyethylene collar provided with a thread was sutured to the skin surrounding the exteriorized intestine, and a wide-mouth bottle of the same material screwed into the collar.

The hens received the following diet (quantities as percentages):

Table 1

Glucose	59·65	Choline chloride	0·1
Soybean oil meal	20	Vitamin mixtures (ref. 3)	0·25
Dried egg albumen	8	K_2HPO_4	1·1
Refined corn oil	3	NaH_2PO_4, $2H_2O$	1·1
Sodium chloride	0·3	$CaCO_3$	6·5

The assayed calcium and phosphorus contents of the diet were 2·64 and 0·50 per cent, respectively. The feed was supplied *ad libitum* from feeders specially constructed to minimize spillage. Water was supplied by a low-pressure drip system mounted overhead at the rear end of the cage, the 'founts' being activated by contact with the chicken's beak; this system minimizes feed wastage in water[4]. Daily measurements of calcium and phosphorus intake and excretion were done on four surgically prepared hens receiving this diet for seven consecutive days. Calcium was determined by a method using ethylenediamine tetraacetate as described elsewhere[5]. For the estimation of phosphorus the excreta were wet-ashed with 10 *N* sulphuric acid and 30 per cent hydrogen peroxide and phosphorus determined by Gomori's method[6].

The results are summarized in Table 2. The absolute amount of calcium appearing in the urine is similar to the amount of phosphorus, but as a percentage of the ingested mineral, 51 per cent of the ingested phosphorus appeared in the urine, whereas the corresponding average value for calcium was only 7 per cent. More than 58 per cent of the ingested calcium was deposited in the egg (most of it in the shell) and nearly all the calcium retained could be accounted for by the calcium of the egg. As a percentage of excreted mineral, 19 per cent of the excreted calcium and 62 per cent of the excreted phosphorus were found in the urine.

Table 2. Calcium and Phosphorus Balance in Colostomized Hens

	Calcium	Phosphorus
	(gm./hen/day)	
Consumption	3·00 ± 0·06*	0·57 ± 0·12
Excretion in faeces	0·95 ± 0·21	0·18 ± 0·03
Absorption†	2·05 ± 0·58	0·39 ± 0·12
Excretion in urine	0·22 ± 0·06	0·29 ± 0·02
Retention‡	1·83 ± 0·56	0·10 ± 0·10
Eggs§	1·75 ± 0·17	0·08 ± 0·00
Balance	0·08 ± 0·15	0·02 ± 0·02
	(Per cent)	
Absorption†	67·8 ± 9·9	67·0 ± 8·1
Retention‡	60·4 ± 10·7	15·5 ± 14·6

* Arithmetic mean ± standard deviation, calculated from individual values (4 hens for 7 days).

† Apparent absorption (consumption minus faecal excretion) disregarding possible re-excretion of absorbed calcium and phosphorus into the gastro-intestinal tract.

‡ Consumption minus excretion in urine and faeces.

§ Each hen laid six eggs during the seven-day experimental period. The figures for eggs (and balance) denote the total values of the period divided by seven; the standard deviations are based on the averages for each hen thus obtained.

The average apparent absorption was similar for both calcium and phosphorus. It should be kept in mind, however, that the true absorption is probably higher, since the possibility of re-excretion of absorbed minerals into the intestinal tract must be considered. On the other hand, the retention and percentage retention of phosphorus were much lower than that of calcium, and showed a relatively higher variability. This higher variability of phosphorus retention may be connected with the need of the individual bird to draw upon bone material. Since the ratio calcium/phosphorus in bone (2·5 : 1) differs greatly from that required for egg formation (20 : 1), hens having a negative calcium balance, indicating the use of bone calcium for egg formation, are likely to have an excess of phosphorus at their disposal; this will lead to an increased urinary excretion of phosphorus and consequently a low retention of phosphorus, as calculated on the balance sheet. In fact, the only hen on a negative calcium balance (−0·08 gm.) in this experiment excreted as much as 0·35 gm. phosphorus/day and retained only 0·03 gm.

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RADIOBIOLOGY

Protective Action of Calcium Gluconate against After-effects of X-irradiation on Conidia of *Neurospora crassa*

An increase in the survival of conidia of *Neurospora crassa* irradiated with X-rays has been found when calcium gluconate is added to the plating medium.

A colonial, microconidial, fluffy strain of *N. crassa* (*FC*4–51) was grown on a minimal Vogel medium[1] containing 1 mgm. of calcium chloride per 10 ml. Conidia were harvested after incubation for seven days at 30° C. and suspended in distilled water with a final density of 5×10^6 cells per ml. Seven (10 ml.) samples were exposed to X-ray doses of 240, 720, 1,200, 2,400, 7,200 and 9,600 r. respectively (dose-rate 4 r./sec. at a distance of 25 cm. from the target of a Philips X-ray machine operating at 300 kV. constant potential, with a half-value thickness for the unfiltered beam of 5 mm. aluminium). The conidia from both the irradiated and control samples were plated on minimal medium with and without added calcium gluconate (15 mgm./10 ml.). The amount of light received by the conidia during plating was kept to a minimum and constant for all samples. Six replicate experiments were carried out at each dose. After plating, the conidia were incubated at 30° C. in darkness and germination counts were made on the fifth day.

The addition of calcium gluconate caused an increase in the germination of irradiated conidia when compared with that on the unsupplemented medium (Table 1). This increase in survival was observed at all dose-levels studied and was statistically

Table 1. Effect of Calcium Gluconate on the Percentage Survival of Conidia of *Neurospora crassa* Irradiated at Different Dose-Levels

Dose-level (r.)	Germination of irradiated sample on minimal medium*	Germination of irradiated sample on minimal medium + calcium gluconate*	
0	100	98	
50	132†	196†	$P < 0{\cdot}001$
240	76	151†	$P < 0{\cdot}001$
720	46	96	$P < 0{\cdot}001$
1,200	93†	98	$P < 0{\cdot}8$
2,400	59	92	$P < 0{\cdot}001$
4,800	34	79	$P < 0{\cdot}001$
7,200	44	78	$P < 0{\cdot}001$
9,600	40	76	$P < 0{\cdot}001$

* Normalized to germination of unirradiated control conidia as 100. The irradiation experiments with different doses of X-rays consisted of six replicates, each replicate representing 40 conidial platings with a colony count of approximately 100 colonies per plate at zero *r*. The plating efficiencies of all 96 replicates were determined before irradiation, but these results have not been incorporated in this table, no significant differences ($P > 0{\cdot}01$) having been observed.
† These figures were consistently high in all six replicates.

significant ($P = 0{\cdot}05$) in seven out of eight doses. The presence of calcium gluconate after irradiation, therefore, lessened the death-rate of spores. Unirradiated conidia showed no significant difference in germination on the two media.

The plating efficiency of the unirradiated conidial cells is about 35 per cent. The germination of treated conidia has been expressed as a percentage of the germination of unirradiated control conidia. Thus, an increase in plating efficiency as a result of the treatments may appear as a germination percentage of greater than 100.

In addition to the protective action of calcium against the consequences of radiation injury, there was also evidence at certain doses of stimulation of germination by the radiation. In some cases this was seen as an increased efficiency of plating when compared with that at zero dose; in others it was apparent as a reduction in net death of conidia compared with that observed following lower doses (unpublished work). Thus, when conidia were plated on minimal medium without calcium gluconate, the survival percentage following a 50 r. exposure exceeded 100, and survival following a 1,200 r. exposure (while less than that at zero dose) was twice as great as at 720 r. The survival steadily decreased at doses higher than 7,200 r. (zero survival out of 10^6 conidia being obtained with 115,000 r.). Superimposed on the destructive effects of the irradiation there is apparently stimulation induced by radiation of conidia which would not otherwise germinate.

Rixon and Whitfield[2], in work involving increased survival of X-irradiated rats when treated with parathyroid extract, stated that protection against radiation death might be due to the ability of the hormone to increase serum calcium; they (Whitfield and Rixon, personal communication) believe that an increased calcium-level protects the irradiated cell by reducing leakage of cell components through the cell membrane.

The radiation experiments with conidia of *N. crassa* confirm the hypothesis that calcium is a potential protector against death arising from the effects of radiation, and the experiments reported below show that the protection is associated with the prevention of a radiation-induced increase in cell permeability.

Conidia were raised on a medium containing 1·5 mc. of phosphorus-32 per agar slant for 7 days.

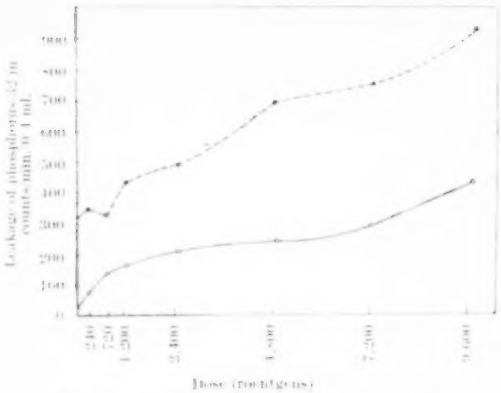

Fig. 1. Protective action of calcium gluconate against leakage of phosphorus-32 from conidia of *Neurospora crassa* after X-ray irradiation. ——, untreated; ————, treated with calcium gluconate

By the end of this time, there was 10^{-3} gm. phosphorus-32/conidium. When these conidia were irradiated, there was a rapid release of phosphorus-32 into the medium (distilled water) in which the conidia were suspended. The magnitude of this leakage varied with the dose (Fig. 1).

When calcium gluconate was added to the medium on which the conidia were raised (25 mgm. 10 ml. medium) (Fig. 1), and also when it was added to the distilled water in which the conidia were irradiated, the post-radiation leakage of phosphorus-32 could be largely prevented even when X-ray doses as high as 7,200 r. were used.

A detailed report of these experiments will be published later. The work was carried out in part during the tenure of a visiting professorship at the Biology Branch of Atomic Energy of Canada, Ltd., Chalk River (Ontario), and was supported in part by a research grant from the National Cancer Institute of Canada. My thanks are due to Dr. J. F. Whitfield and Dr. R. H. Rixon for their interest during these investigations.

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Protective Effects of Diisopropylfluorophosphonate against the Lethal Effects of X-rays before or after Irradiation

Pre-treatment with di*iso*propylfluorophosphonate (DFP) suppresses the increase in permeability of the intestinal vessels of rats after abdominal irradiation[1,2] and similar vascular changes due to other types of injury[3]. DFP also reduces gastrointestinal symptoms (diarrhœa), which occur after exposure to X-rays. Since death from gastrointestinal injury is one of the well-recognized forms of acute radiation death, it was decided to test the effects of DFP on rats exposed to whole-body irradiation. Twenty rats were given 975 r. whole-body X-rays with a Philips X-ray apparatus (200 kV., 15 m.amp., 0·5 mm. copper, and 1·0 mm. aluminium filters, *F.S.D.* 30 cm. distance); ten of these animals received a prior injection of DFP before irradiation (3·0 mgm./kgm.).

The results of this experiment (Fig. 1) show that in the first three days after exposure to X-rays 60 per cent of the control, but only 20 per cent of the pre-treated animals had died. By 28 days, however, the same proportion of control and pre-treated animals survived. The early deaths (up to three days) were due to gastrointestinal injuries which manifested themselves in severe diarrhœa and its consequences, while the deaths in the second phase (six days and later) could be attributed to the lethal injuries to the haematopoietic system, thus confirming the well-established sequence of radiation deaths[4,5].

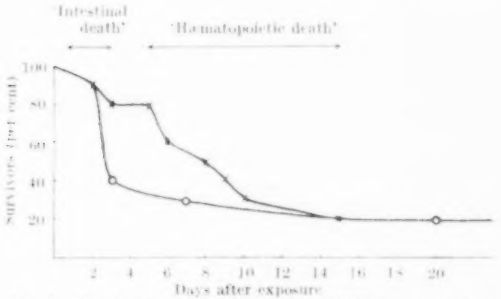

Fig. 1. Effect of DFP on whole-body irradiation. ●, treated with DFP; ○, X-rays only

Thus it appears that pre-treatment with DFP protected the rats against the 'intestinal death' but not the 'haematopoietic death'. To test this hypothesis further, rats were irradiated with various doses of X-rays over the entire abdomen, the rest of the animal being shielded so that most of the haematopoietic system was protected.

Table 1 indicates that treatment with DFP not only delays but also prevents death in a high percentage of rats exposed to doses of 1,050–1,334 r. of half-body irradiation. Of 60 rats receiving such doses of X-rays 95 ± 2·8 per cent died within four weeks, while of those treated with DFP only 65 ± 6·2 per cent succumbed (difference 30 ± 6·8). DFP proved ineffective when the dose of X-rays was increased to 2,200 r. The protective effect of DFP was the same whether administered before, immediately after exposure or 24 hr. after irradiation (Table 1).

Table 1. Effect of DFP Treatment on the Survival of Irradiated Rats (Abdominal Fields)

Dose (r.)	No. of rats	DFP treatment	Time to reach 50 per cent deaths (days)	Per cent deaths at 7 days	Per cent deaths at end of experiment (28 days)
1,050	12	0	5·5	58·0	82·5
1,050	12	0	4·0	75·0	100·0
1,050	12	Before X-rays	11·5	25·0	58·0
1,050	12	Before X-rays	11·0	25·0	58·0
1,050	12	0	5·0	75·0	92·0
1,050	12	Immediately after X-rays	11·0	33·0	58·0
1,334	12	0	3·0	92·0	100·0
1,334	12	Before X-rays	4·5	66·0	75·0
1,334	12	0	3·0	92·0	100·0
1,334	12	24 hr. after X-rays	5·5	50·0	75·0
2,200	12	0	3·5	100·0	100·0
2,200	12	Before X-rays	4·0	92·0	92·0

The average apparent absorption was similar for both calcium and phosphorus. It should be kept in mind, however, that the true absorption is probably higher, since the possibility of re-excretion of absorbed minerals into the intestinal tract must be considered. On the other hand, the retention and percentage retention of phosphorus were much lower than that of calcium, and showed a relatively higher variability. This higher variability of phosphorus retention may be connected with the need of the individual bird to draw upon bone material. Since the ratio calcium/phosphorus in bone (2·5 : 1) differs greatly from that required for egg formation (20 : 1), hens having a negative calcium balance, indicating the use of bone calcium for egg formation, are likely to have an excess of phosphorus at their disposal; this will lead to an increased urinary excretion of phosphorus and consequently a low retention of phosphorus, as calculated on the balance sheet. In fact, the only hen on a negative calcium balance (−0·08 gm.) in this experiment excreted as much as 0·35 gm. phosphorus/day and retained only 0·03 gm.

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RADIOBIOLOGY

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* Normalized to germination of unirradiated control conidia as 100. The irradiation experiments with different doses of X-rays consisted of six replicates, each replicate representing 40 conidial platings with a colony count of approximately 100 colonies per plate at zero r. The plating efficiencies of all 96 replicates were determined before irradiation, but these results have not been incorporated in this table, no significant differences ($P > 0{\cdot}01$) having been observed.
† These figures were consistently high in all six replicates.

significant ($P = 0{\cdot}05$) in seven out of eight doses. The presence of calcium gluconate after irradiation, therefore, lessened the death-rate of spores. Unirradiated conidia showed no significant difference in germination on the two media.

The plating efficiency of the unirradiated conidial cells is about 35 per cent. The germination of treated conidia has been expressed as a percentage of the germination of unirradiated control conidia. Thus, an increase in plating efficiency as a result of the treatments may appear as a germination percentage of greater than 100.

In addition to the protective action of calcium against the consequences of radiation injury, there was also evidence at certain doses of stimulation of germination by the radiation. In some cases this was seen as an increased efficiency of plating when compared with that at zero dose; in others it was apparent as a reduction in net death of conidia compared with that observed following lower doses (unpublished work). Thus, when conidia were plated on minimal medium without calcium gluconate, the survival percentage following a 50 r. exposure exceeded 100, and survival following a 1,200 r. exposure (while less than that at zero dose) was twice as great as at 720 r. The survival steadily decreased at doses higher than 7,200 r. (zero survival out of 10^8 conidia being obtained with 115,000 r.). Superimposed on the destructive effects of the irradiation there is apparently stimulation induced by radiation of conidia which would not otherwise germinate.

Rixon and Whitfield[2], in work involving increased survival of X-irradiated rats when treated with parathyroid extract, stated that protection against radiation death might be due to the ability of the hormone to increase serum calcium; they (Whitfield and Rixon, personal communication) believe that an increased calcium-level protects the irradiated cell by reducing leakage of cell components through the cell membrane.

The radiation experiments with conidia of *N. crassa* confirm the hypothesis that calcium is a potential protector against death arising from the effects of radiation, and the experiments reported below show that the protection is associated with the prevention of a radiation-induced increase in cell permeability.

Conidia were raised on a medium containing 1·5 mc. of phosphorus-32 per agar slant for 7 days.

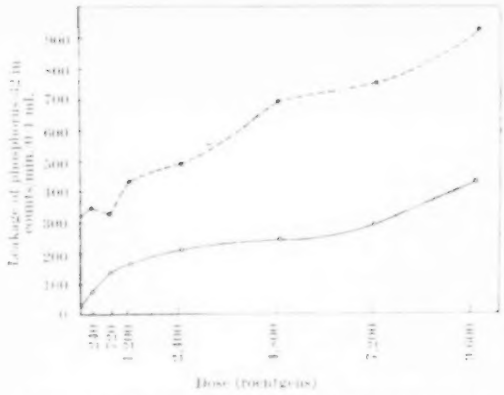

Fig. 1. Protective action of calcium gluconate against leakage of phosphorus-32 from conidia of *Neurospora crassa* after X-ray irradiation. ——, untreated; - - - - -, treated with calcium gluconate

By the end of this time, there was 10^{-3} gm. phosphorus-32 conidium. When these conidia were irradiated, there was a rapid release of phosphorus-32 into the medium (distilled water) in which the conidia were suspended. The magnitude of this leakage varied with the dose (Fig. 1).

When calcium gluconate was added to the medium on which the conidia were raised (25 mgm./10 ml. medium) (Fig. 1), and also when it was added to the distilled water in which the conidia were irradiated, the post-radiation leakage of phosphorus-32 could be largely prevented even when X-ray doses as high as 7,200 r. were used.

A detailed report of these experiments will be published later. The work was carried out in part during the tenure of a visiting professorship at the Biology Branch of Atomic Energy of Canada, Ltd., Chalk River (Ontario), and was supported in part by a research grant from the National Cancer Institute of Canada. My thanks are due to Dr. J. F. Whitfield and Dr. R. H. Rixon for their interest during these investigations.

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Protective Effects of Diisopropylfluorophosphonate against the Lethal Effects of X-rays before or after Irradiation

Pre-treatment with di*iso*propylfluorophosphonate (DFP) suppresses the increase in permeability of the intestinal vessels of rats after abdominal irradiation[1,2] and similar vascular changes due to other types of injury[3]. DFP also reduces gastrointestinal symptoms (diarrhœa), which occur after exposure to X-rays. Since death from gastrointestinal injury is one of the well-recognized forms of acute radiation death, it was decided to test the effects of DFP on rats exposed to whole-body irradiation. Twenty rats were given 975 r. whole-body X-rays with a Philips X-ray apparatus (200 kV. 15 m.amp. 0·5 mm. copper, and 1·0 mm. aluminium filters, *F.S.D.* 30 cm. distance); ten of these animals received a prior injection of DFP before irradiation (3·0 mgm./kgm.).

The results of this experiment (Fig. 1) show that in the first three days after exposure to X-rays 60 per cent of the control, but only 20 per cent of the pre-treated animals had died. By 28 days, however, the same proportion of control and pre-treated animals survived. The early deaths (up to three days) were due to gastrointestinal injuries which manifested themselves in severe diarrhœa and its consequences, while the deaths in the second phase (six days and later) could be attributed to the lethal injuries to the haematopoietic system, thus confirming the well-established sequence of radiation deaths[4,5].

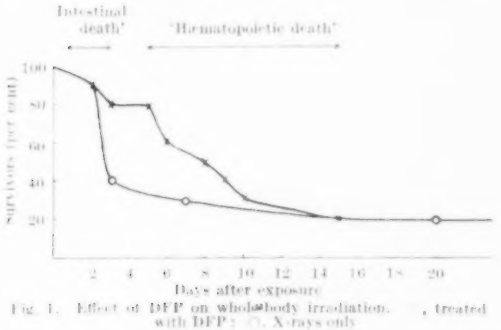

Fig. 1. Effect of DFP on whole-body irradiation. ●——●, treated with DFP; ○——○, X-rays only

Thus it appears that pre-treatment with DFP protected the rats against the 'intestinal death' but not the 'haematopoietic death'. To test this hypothesis further, rats were irradiated with various doses of X-rays over the entire abdomen, the rest of the animal being shielded so that most of the haematopoietic system was protected.

Table 1 indicates that treatment with DFP not only delays but also prevents death in a high percentage of rats exposed to doses of 1,050–1,334 r. of half-body irradiation. Of 60 rats receiving such doses of X-rays 95 ± 2·8 per cent died within four weeks, while of those treated with DFP only 65 ± 6·2 per cent succumbed (difference 30 ± 6·8). DFP proved ineffective when the dose of X-rays was increased to 2,200 r. The protective effect of DFP was the same whether administered before, immediately after exposure or 24 hr. after irradiation (Table 1).

Table 1. Effect of DFP Treatment on the Survival of Irradiated Rats (Abdominal Fields)

Dose (r.)	No. of rats	DFP treatment	Time to reach 50 per cent deaths (days)	Per cent deaths at 7 days	Per cent deaths at end of experiment (28 days)
1,050	12	0	5·5	58·0	82·5
1,050	12	0	4·0	75·0	100·0
1,050	12	Before X-rays	11·5	25·0	58·0
1,050	12	Before X-rays	11·0	25·0	58·0
1,050	12	0	5·0	75·0	92·0
1,050	12	Immediately after X-rays	11·0	33·0	58·0
1,334	12	0	3·0	92·0	100·0
1,334	12	Before X-rays	4·5	66·0	75·0
1,334	12	0	3·0	92·0	100·0
1,334	12	24 hr. after X-rays	5·5	50·0	75·0
2,200	12	0	3·5	100·0	100·0
2,200	12	Before X-rays	4·0	92·0	92·0

These experiments support the theory that DFP selectively protects rats from 'acute intestinal death' even if given *after* exposure to irradiation.

I am grateful to Dr. H. B. Fell and Dr. A. Glucksmann for their advice and encouragement. This work was done at the Strangeways Research Laboratory, Cambridge, during the tenure of a Wellcome Research Scholarship.

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Differential Radiosensitivity in Rice (*Oryza sativa* Linn.) at the Genotypic Level

Information on differential radiosensitivity of genotypes of a gene locus is scanty[1]. During a course of investigations on the effects of pile radiation on rice, advantage was taken of an anthocyanin pigmented mutant appearing as a heterozygote for albinism in N_1 population of a variety *GEB-24* to study the relative radiosensitivity of the genotypes at this locus. N_2 seedlings of the mutant segregated into greens and albinos in a 3 : 1 ratio. N_3 plants, homozygous dominant and heterozygous for chlorophyll character, segregated in 1 : 2 ratio, showing that the genes for albinism behaved as simple recessive to normal green. In the first of the two experiments, dry seeds from the heterozygous N_1 plant were irradiated with 5–40 kr. of X-rays from a therapy type X-ray machine operating at 250 kV., 30 m.amp., with 2·0 mm. copper. The seeds, stabilized for moisture content, were placed at a distance of 22·0 cm. from the target and at that distance the dose-rate was 309 r. per min. In the second experiment, in addition to those from the N_1 plant referred to above, seeds of one of its N_2 progeny, known to be homozygous dominant for green, were also irradiated. The dosage-range was 10–50 kr., and the dose-rate at a distance of 13·5 cm. from the target was 650 r. per min.

It can be seen from Table 1 that X-ray doses higher than 20 kr. had increasing effects on the rate of reduction of number of seedlings in both the experiments. It was further evident that with high doses the normal ratio, namely, 3 : 1 of green to albino seedlings, was also affected. As the dose increased, the rate of decrease of albinos in relation to greens became significantly higher, giving eventually 9 : 1 and 9·5 : 1 ratios for greens to albinos at 40 kr. in experiments 1 and 2 respectively (Fig. 1). It was evident that this was due to the greater lethality in the albinos, and the seeds carrying the recessive condition were more radiosensitive than the other two genotypes. It is of further interest to note that a difference existed between the homo- and heterozygotes for green in their degree of radiosensitivity. At the dose-level of 40 kr., there was more than four-fold decrease in emergence of seedlings in the mixed population of homo- and heterozygous greens as compared to the homozygous dominant. Presumably the greater radiosensitivity of the recessive gene is expressed even when it is in a heterozygous condition. Whether higher radiosensitivity in the recessive genotype was due to a pleiotropic effect or mutation of a closely linked gene

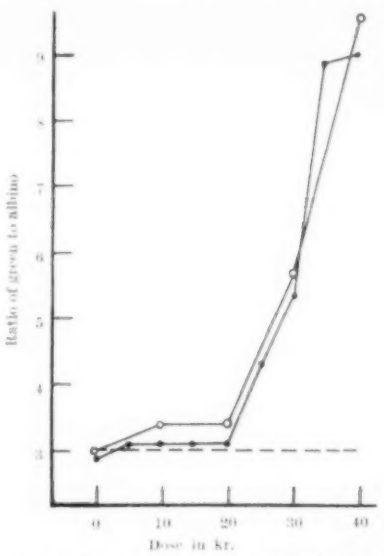

Fig. 1. Ratio of green to albino: ——, expected; ●—●—●, observed in exp. 1; ○—○—○, observed in exp. 2

Table 1. Effect of X-Rays on Emergence of Rice seedlings
Material, *O. sativa*, var. *GEB-24*. Total number of seeds irradiated per treatment: Exp. 1, 400; Exp. 2, 200

Treatments	Exp. 1 No. of seedlings from the N_1 plant 14 days after sowing				Exp. 2 No. of seedlings from the N_1 plant 21 days after sowing				No. of seedlings from an N_2 plant 21 days after sowing
	Percentage emergence of: homo- and hetero-zygous greens	albinos	χ^2	P*	Percentage emergence of: homo- and hetero-zygous greens	albinos	χ^2	P*	Percentage emergence of homozygous green
Control	73·7	24·7	0·003	0·99	69·0	23·0	0	0·99	99·0
5 kr.	64·0	20·5	0·098	0·90–0·80	—	—	—	—	—
10 kr.	70·2	22·7	0·057	0·90–0·80	65·5	19·5	0·384	0·70–0·50	97·5
15 kr.	71·7	23·0	0·106	0·80–0·70	—	—	—	—	—
20 kr.	67·7	21·2	0·239	0·70–0·50	62·5	18·5	0·403	0·70–0·50	97·0
25 kr.	64·0	14·0	8·274	0·01–0·001	—	—	—	—	—
30 kr.	61·0	11·5	14·405	< 0·001	46·0	8·0	5·975	0·02–0·01	85·0
35 kr.	42·5	4·7	22·520	< 0·001	—	—	—	—	—
40 kr.	27·0	3·0	14·400	< 0·001	9·5	1·0	2·682	0·20–0·10	63·0
50 kr.	—	—	—	—	0	0	—	—	0

* Probability of obtaining a ratio different from 3 : 1.

or albinism *per se* could not be ascertained from the present observations.

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Metabolism of Carboxyl-^{14}C-labelled 2,4-Dichlorophenoxyacetic Acid by Bean Stems: Heterogeneity of the Ethanol-soluble, Ether-insoluble Products

There is a considerable disagreement in the literature concerning the nature and number of radioactive metabolites which can be isolated from bean plants following exposure to 2,4-dichlorophenoxyacetic acid (2,4-D) labelled with carbon-14 (refs. 1–6). Because of this situation it was decided to re-investigate this problem in connexion with our work on the induction of callus growth in bean stem sections by 2,4-D (ref. 7).

The details of the preparation and isolation of the radioactive, water-soluble products from bean stems which were treated with carboxyl-^{14}C-2,4-D will be reported elsewhere. Briefly, bean stems were vacuum infiltrated with 2 per cent sucrose and 10^{-4} *M* carboxyl-^{14}C-2,4-D (2 mc./m*M*), surface sterilized by brief immersion in 0·5 per cent sodium hypochlorite solution, rinsed in sterile distilled water, and incubated in nutrient medium for 2 days. They were lyophilized, pulverized, and continuously extracted with wet acetonitrile. After removal of the solvent by distillation, ether-soluble material was extracted at *p*H 1·5, and sedimenting insoluble matter discarded. The aqueous layer was chromatographed on a 'Dowex-1' formate column using a gradient of increasing formic acid concentration. The radioactive peak was freed from formic acid and further purified by passage through a water-saturated silicic acid column using water-saturated 35 per cent *n*-butanol in chloroform as the eluting agent. The product was homogeneous by paper chromatography in the solvent of Jaworski *et al.*[4] and contained no detectable ninhydrin-positive contaminants.

When this material was absorbed on to a small amount of charcoal ('Nuchar') in a sintered glass funnel, the elution pattern shown in Table 1 was obtained. Separate re-application of each of these four fractions to fresh charcoal resulted in their elution at the same relative positions. When another aliquot of the purified material was applied to a charcoal column which differed from that described by Stambaugh and Wilson[8] only in that the column was doubled in length while column diameter and volume of eluting solvent were halved, the distribution of radioactivity shown in Fig. 1 was obtained. This pattern was very reproducible and suggests the presence of some 10 different components in this mixture. In practice, it was found that not all

Table 1. Elution of Purified Radioactive, Water-soluble and Ether-insoluble Bean Extract from 'Nuchar'

A total of 3,000 c.p.m. were applied to 0·5 gm. charcoal. Three 10-ml. fractions were collected with each solvent

Solvent	Total c.p.m. eluted
Water	144
25 per cent ethanol (aqueous)	763
1 per cent NH_4OH in 25 per cent aqueous ethanol	1,496
50 per cent aqueous acetonitrile	306
Total recovered	2,709

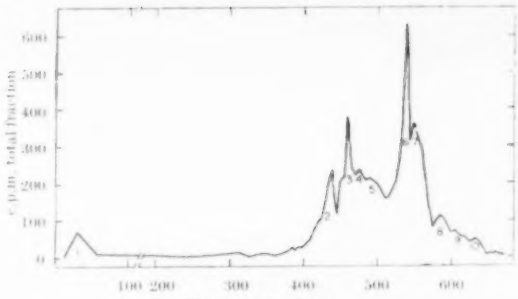

Fig. 1. The elution of radioactivity from 12-in. charcoal columns. 5 ml. fractions were cut between 350 and 700 ml. eluted volume

these materials were equally stable, and if great care was not taken during the chromatography on 'Dowex-1', there was considerable hydrolysis, resulting in the release of some radioactivity in ether-soluble form accompanied by the appearance of at least 10 distinct ninhydrin-positive materials in the water-phase. The remaining water-soluble radioactivity was eluted from charcoal only with 1 per cent ammonium in 25 per cent ethanol.

Holley[2] suggested that the ether-soluble hydrolysis product of the water-soluble bean fraction might be 6-OH-2,4-D, even though the compound was unknown at that time. Since then, 6-OH-2,4-D has been prepared by Cavill and Ford[9,7]. Using a small sample of this material, generously supplied by Dr. D. L. Ford, we found that it travels on paper indistinguishably from 2,4-D in the solvents previously used. However, when methylethylketone–conc. ammonium–water (100 : 5 : 3·2 v/v/v) was used the two compounds were readily separated. In this solvent the ether-soluble radioactive hydrolysis product from the bean extract was clearly separated from both these known substances (R_F : 2,4-D = 0·35; 6-OH-2,4-D = 0·61; bean extract hydrolysate = 0·0). Counter-current distribution of the ether-soluble material at *p*H 5·1 between phosphate buffer and diethylether resulted in the separation of four radioactive components. These results suggest that the previously reported main product of 2,4-D metabolism in beans[1–4] is indeed a complex mixture of amino-acid amides of several different and as yet unknown acid metabolites of 2,4-D. Further work towards the identification of these acids is in progress.

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Excretion and Hepatic Storage of 5,6-Dimethylbenziminazolyl Cobamide Coenzyme labelled with Cobalt-58

BARKER *et al.*[1,2] recently isolated a number of vitamin B_{12} derivatives from bacteria and demonstrated that they act as coenzymes in the conversion of glutamate to β-methylaspartate. Since the 5,6-dimethylbenziminazolyl cobamide coenzyme (DCC) was found to occur in rabbit liver[2], and to act as a co-factor in a rat enzyme system[3], it is reasonable to assume that the coenzymes are the forms in which vitamin B_{12} exists in the tissues and that the 'extrinsic factor' may largely consist of DCC and similar compounds. Since we have previously been engaged in research on the turnover of vitamin B_{12} (refs. 4 and 5), we thought it of interest to perform similar work on the turnover of radioactive DCC in man.

Four healthy student nurses who volunteered for the experiment were given an intragluteal injection of DCC labelled with cobalt-58. The preparation was kindly provided by the Squibb Institute for Medical Research, New Brunswick, New Jersey, and had a specific activity of about 1 μc. per μgm. The radioactive DCC was injected soon after its arrival from abroad and protected from light in order to minimize breakdown.

Three of the test subjects received a dose of 1 μgm. and one 0·75 μgm. in 1 ml. of physiological saline. The test subjects collected their excreta in one-day portions for 39 days (except on days off), and later faeces only during the seventieth to seventy-ninth day following the injection. The samples of faeces were incinerated at 600–800° C. in porcelain cups in a coal furnace in the boiler room of the hospital. Recovery experiments demonstrated that no loss of radioactivity occurred during this procedure. The urine samples were concentrated by evaporation. The ashes and the concentrates were counted in a well-type scintillation counter together with appropriate standards, and the radioactivity was expressed as mμgm. of the injected DCC.

Radioactivity counts were also taken over the liver area under standard conditions, once a day for the first 39 days, and once on the sixty-fifth day. The counts were corrected for radioactive decay.

The results of the excretion work are given in Table 1. It is seen that during the first few days after the injection the urinary excretion was slightly elevated, but later on the excretion of radioactivity was remarkably constant. From the fifth day on, urinary and faecal excretions were about equal. The fraction of the total-body radioactivity lost per day was about 0·3 per cent or slightly less. This value corresponds to a biological half-life of about one year.

From the first day following the injection, relatively strong radioactivity was measured over the liver area, the counts ranging from 246 to 828 c.p.m. above the background (~410 c.p.m.). Maximum counts were observed within the first 12 days. During the 65-day period when liver counts were taken, there was no clear-cut decrease in hepatic radioactivity. Thus the hepatic biological half-life must be long.

On the whole, the results obtained with radioactive DCC are very similar to those observed after administration of radioactive vitamin B_{12}[4,6–8]. When radioactive DCC is injected there is possibly slightly less 'spill-over' of radioactivity into the urine in the days immediately following the injection. During later periods the excretion-rates and the total-body biological half-lives of the two compounds are very similar.

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Table 1. MEAN DAILY EXCRETION OF RADIOACTIVITY

The radioactivity is expressed as mμgm. of the injected preparation. *F*, faeces; *U*, urine; %, sum of faecal and urinary excretions expressed as percentage of the radioactivity estimated to be contained in the body at the time of excretion.

Case Injected dose	*A* 1 μgm.			*B* 1 μgm.			*C* 1 μgm.			*D* 0·75 μgm.		
	F	*U*	%	*F*	*U*	%	*F*	*U*	%	*F*	*U*	%
1st–4th day	0·4	6·2	0·68	2·2	5·1	0·75	0·3	5·9	0·64	0·6	3·7	0·59
5th–39th day	1·5	1·1	0·28	1·0	1·4	0·26	1·0	1·4	0·26	1·1	1·1	0·32
70th–79th day	1·3	1·0*	0·29	1·2	1·7*	0·38	—	—	—	0·7	0·7*	0·24

* Because quantitative collection of urine for long periods is difficult, the subjects collected only faeces during this period. The urinary excretion was estimated on the assumption that the *U* : *F* ratio was the same as during the preceding collection period.

HÆMATOLOGY

Occurrence of Heparin in the Blood of Fish and its Prevention of the Clotting of Fish Plasma

THE property of the blood of fish to clot rapidly provides a means of protection from fatal haemorrhage such as may follow injuries[1]. Sometimes in the same fish the blood clotting-time is known to differ markedly at two different phases of its life-cycle. In the pre-spawning phase when the fish is fully laden with reserves, blood clotting is almost instantaneous, whereas during the period of physiological stress which generally follows spawning, clotting is slow and prolonged. Such variations in the coagulation-time have been attributed to some unknown factors which may involve a change in the chemistry of the blood of fishes[2].

Heparin, the well-known anticoagulant, is a polysulphuric acid ester of a polysaccharide[3]. It has the remarkable property of preserving the fluidity of blood both *in vitro* and *in vivo*[4]; and for this reason in recent years there has been increasing recognition of its value in medicine and surgery[5]. The presence of heparin has generally been recorded in the blood and tissues of homoiothermous animals such as mammals which form the chief source for its extraction[6]. In poikilothermous animals and more particularly in fishes there appears to be no previous account of its occurrence and mode of action.

During a study of the haematology of the Indian freshwater murrel *Ophicephalus punctatus* (Bloch), blood samples were collected with a hypodermic syringe from the truncus arteriosus after pithing the fishes and exposing the heart. It then appeared that the clotting time of blood was short and that without the use of anticoagulants, suitable samples could not be obtained. A solution of peptone, as used by earlier workers in higher animals[7], was injected to liberate excessive quantities of heparin *in vivo*. This gave satisfactory results as the blood lost the power of clotting temporarily although the peptone solution in itself did not prevent clotting *in vitro*. It thus became evident that even in fishes production of heparin in order to maintain the fluid nature of blood was a natural phenomenon. Further tests were carried out to illustrate the presence of heparin in blood and its capacity to prevent the clotting of plasma.

Table 1

	Species: *Ophicephalus punctatus*		
	Normal	2 hr. after peptone injection	2 hr. after heparin injection
Prothrombin time at 37° C.	29·4 sec.	58·32 sec.	4 min. 42·5 sec.
Test with toluidine blue	Faintly positive	Positive	Strongly positive

Table 1 gives the plasma prothrombin time of *O. punctatus* by using standard methods[8] under the different conditions. The results indicate that the prothrombin time was prolonged after injecting 0·5 ml. of 5 per cent peptone solution per 100 gm. body-weight. It was considerably longer when the fishes were heparinized with 0·1 ml., heparin B.P., 1,000 I.U. per ml. for every 100 gm. body-weight. In both these cases intramuscular injections were given on the back. Each value given in Table 1 was obtained by using 10 individuals which each gave 2–3 readings. Tests with toluidine blue, as have been recommended for heparin[9], also gave positive results (Table 1).

It therefore seems certain that this remarkable anticoagulant occurs in the blood and possibly in other fish tissues also. It would be interesting to have more information about the piscine mast cells and their occurrence in various tissues, for these cells in other animals are known to secrete heparin[10]. The mechanism of action of heparin in fishes seems similar to that in higher animals[11]. It partly prevents the conversion of prothrombin to thrombin and partly antagonizes the action of thrombin itself. The co-factors such as plasma protein, serum albumin or heparin complement required for the action of heparin seem to be present in fish plasma.

We wish to thank Dr. S. Hameed, pathologist in the Institute of Ophthalmology of this University, for his help.

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A New Hæmoprotein with a Unique Iron Porphyrin Prosthetic Group isolated from Human Erythrocytes

Hæmoglobin, comprising more than 95 per cent of the protein of the red cell, is the major protein in the mature human erythrocyte. The extremely high concentration of this compound in the red cell renders very difficult the identification of other hæmoproteins in the erythrocyte. Catalase is one hæmoprotein which has been isolated from erythrocytes. A third hæmoprotein, spectrally similar to hæmoglobin but which has been reported to be functional in the methæmoglobin reductase system, has also been reported[1,2]. It is the purpose of this communication to present observations on still another hæmoprotein which has been isolated from normal human erythrocytes. This compound is particularly noteworthy since its prosthetic group appears to be different from any previously reported naturally occurring iron porphyrin.

This hæmoprotein can be readily distinguished from hæmoglobin or catalase by its spectral properties as shown in Fig. 1. In its oxidized form the compound has no sharp absorption peaks in the visible region while in the Soret region of the spectra it has a typical hæmoprotein absorption with a maximum at 416 mμ. The cyanide derivative of this compound has a broad peak in the visible region with a maximum at 560 mμ and in the Soret region the peak is at 424 mμ. In contrast to catalase, the new hæmoprotein can readily be reduced with dithionite. The reduced form has absorption maxima at 560 mμ and 434 mμ.

Table 1 compares the position of the absorption maxima of the hæmoproteins known to occur in the red cell. A clear distinction can be made between

Table 1

Hæmoprotein	Oxidized	Absorption maxima		
		Cyanide	Reduced	CO reduced
Preparation	416	424	434	422
Catalase (ref. 6)	407	425	—	—
Myeloperoxidase (ref. 7)	430	458	475	—
Methæmoglobin	405	415	430	418

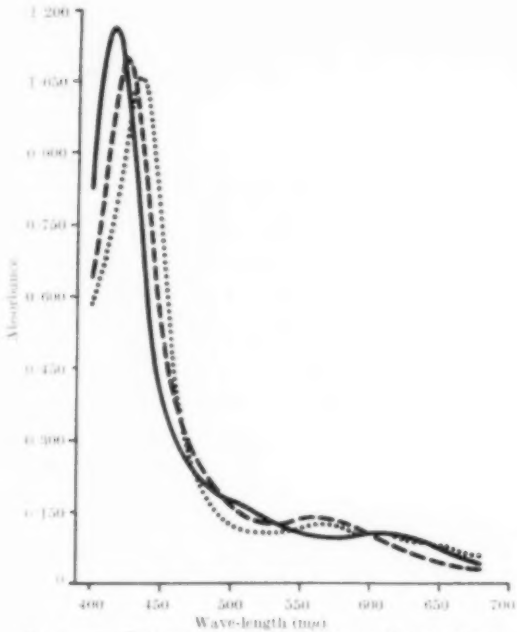

Fig. 1. ——, The haemoprotein is dissolved in 0·1 *M* *tris*(hydroxymethyl) aminomethane buffer *p*H 7·2. The solution contained 2·2 mgm. protein per ml.; . . . . the same preparation as described above to which has been added a few crystals of solid $Na_2S_2O_4$; – – –, the haemoprotein preparation dissolved in 0·1 *M* *tris*(hydroxymethyl) aminomethane containing 0·01 *M* cyanide

the newly isolated haemoprotein and catalase or haemoglobin. It is also easily distinguished from myeloperoxidase, which might conceivably have been present if the white cells had not been completely removed in preliminary stages of the preparation.

The iron porphyrin prosthetic group of this compound appears to differ from that reported for any other haemoprotein. Treatment of the preparation with acidified acetone as previously described[2] does not yield a haemin which is extractable by ether. However, addition of pyridine and alkali to the haemoprotein preparation does yield a haemochromogen spectra. The reduced haemochromogen has an α-peak at 572 mμ, β-peak at 535 mμ and γ-peak at 430 mμ.

A purified preparation of the haemoprotein was analysed for protein by the biuret procedure[4] and the iron content was analysed as previously described[5]. Assuming that each molecule contains a single iron porphyrin moiety, the molecular weight was calculated to be approximately 67,500.

The haemoprotein preparation did not appear to act as a peroxidase. No peroxidase activity could be attributed to the haemoprotein when guiacol, dihydroxyphenylalanine or O-dianisidine were employed as hydrogen donors.

The preparation did not react with reduced di- or tri-phosphopyridine nucleotide. However, the haemoprotein could be reduced by a highly purified reduced triphosphopyridine nucleotide diaphorase (Morrison, M., unpublished work), which was also prepared from the red cells. In enzymatic properties the diaphorase appears to be similar to the methaemoglobin reductase reported by Huennekens *et al.*[1,2] and required methylene blue in order to reduce the haemoprotein. This suggests that the haemoprotein may play some part in electron transport. However, the compound does not have the typical haemochromogen spectra of a cytochrome. It combines with both carbon monoxide and cyanide, which indicates that if its does play a part in electron transport it may act as an oxidase.

The method of preparation and a more detailed account of the characterization of this haemoprotein will be published elsewhere.

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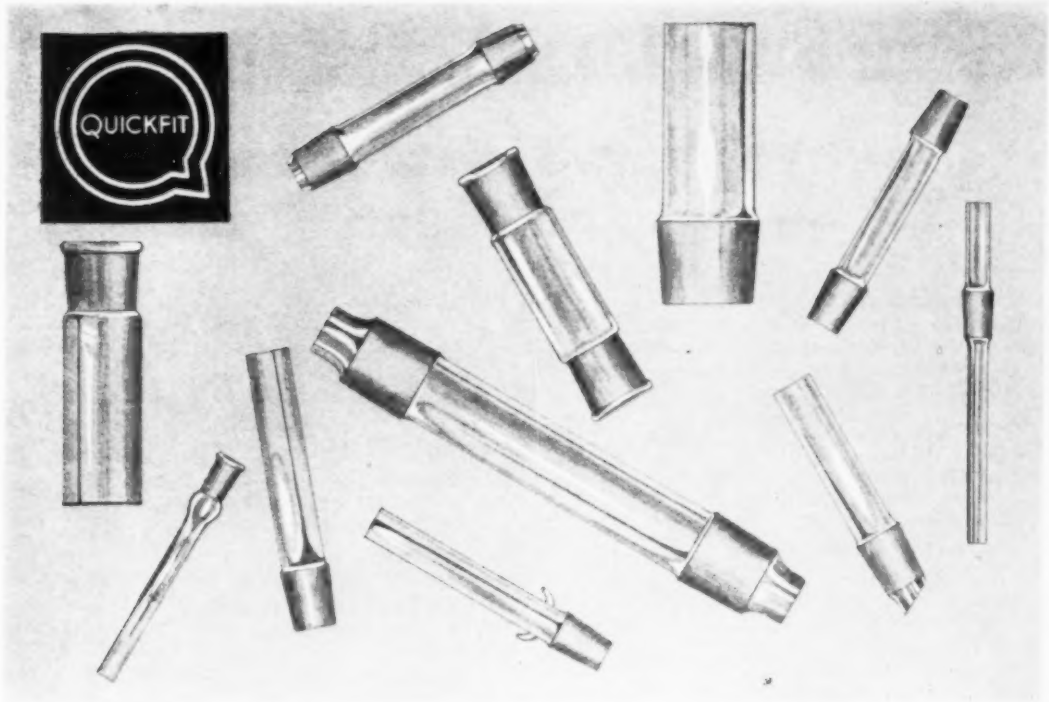
HISTOLOGY

Mast Cells in Peripheral Nerve Trunks

REFERENCES to mast cells occur only rarely in histological accounts of the structure of peripheral nerve trunks. They were mentioned by Cajal[1] and by Riley and West[2] in the perineurium of the rabbit and of the rat respectively, and in the looser connective tissues of the epineurium; they have been described in the endoneurium in the bony fish *Orthagoriscus mola*[3]. In injured nerve trunks, however, Cajal[1] has figured and briefly mentioned mast cells as elements of the endoneurium of the rabbit.

Recently we have studied thin (about 1μ) sections of rat sural and caudal nerves, stained with methylene blue after fixation in Dalton's fluid and embedding in 'Araldite' (a technique recommended to us by Dr. K. C. Richardson). Myelin sheaths, Schwann nuclei, etc., were stained as expected, but, in addition, large cells with metachromatically stained granules were frequently seen in the endoneurium as well as in the perineurium and the epineurium. Metachromatic granules or amorphous material frequently extended from these cells into the nearby tissue spaces between adjacent nerve fibres and as an inner lining to the 'endothelium' of the perineurium. Large metachromatically staining cells of this kind are also conspicuous elements in similarly fixed and stained longitudinal (10μ) sections of cat femoral nerve and mouse sciatic nerve. In the guinea pig sural nerve and in the splanchnic nerves of the rat and man they are also present but in smaller numbers. They are often seen in contact with small nutrient blood vessels, but many occur freely in the endoneurial tissues. In the rat nerves they constitute approximately 1·5–2 per cent of all the cells enclosed within the endothelium of the perineurium. They very closely resemble the mast cells that may be demonstrated in the rat's mesentery by similar fixation and staining or by alcohol fixation and staining with



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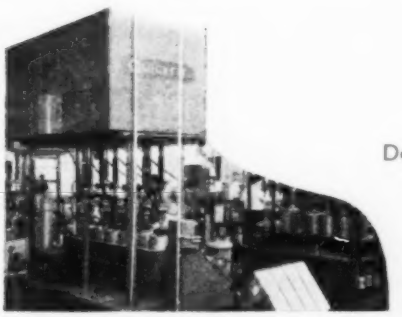

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methylene blue or toluidine blue. For this reason we consider these metachromatically staining cells to be mast cells.

Recent work[4] suggests that some mast cells may be distinguished by their ability to release adrenaline and noradrenaline when suitably stimulated and may be classified as chromaffin cells. The mast cells of rat sural and caudal nerves do not exhibit the 'chromaffin' reaction as this has recently been defined[5], that is, they do not exhibit a yellow coloration after treatment with Orth's fluid. Subsequent staining of the same sections with methylene blue, however, revealed the normal complement of metachromatically stained cells. At the same time, Orth-fixed suprarenal medulla did show the 'chromaffin' reaction in cells which, when stained with methylene blue, did not exhibit metachromasia.

In injured rat nerves some changes occur in the mast cell population, as compared with normal nerves. In nerves cut 1–8 days previously a higher proportion (statistically significant) of the cells appeared to have shed some or many of their granules into the nearby tissue spaces, although the total number present had not changed. In four nerves injured 8 months previously, however, the number of mast cells present had increased about 4 times; in 5 mm. of rat caudal nerve cut, or crushed and allowed to regenerate, as many as 1,250 were counted, as compared with 250–300 in a similar length of normal nerve.

The function of these endoneurial mast cells is at present obscure. In many peripheral nerves a high content of histamine has been recorded[6], and in other tissues this has usually been related to a high content of mast cells[7]. There is also much evidence to implicate mast cells in the elaboration of connective tissue ground substance and, indirectly, of fibrils, although by means as yet unknown[8]. Thus, while mast cell hyperplasia is marked in conditions of fibroplasia, the latter usually appears first. This observation is consistent with the finding of mast cell hyperplasia only in nerves which have degenerated for a long time, where it may be related to the increase in connective tissue collagen reported by Abercrombie and Johnson[9] in such nerves. Mast cells may play some part in the metabolism of endoneurial connective tissue, aiding the formation of fibrils but unable to initiate the process. Their presence may be relevant to the problem of the origin of this tissue, which is by no means satisfactorily solved[10].

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PATHOLOGY

Histochemical Evidence of 5-Hydroxytryptamine in a Dog Mast Cell Tumour

Mast cells of dogs are said not to contain 5-hydroxytryptamine[1–4]. Furthermore, this substance has not been found in neoplasms of these cells in dogs[5]. An instance of a dog mast cell tumour is reported here, however, in which there was histochemical evidence of the presence of 5-hydroxytryptamine.

The tumour removed surgically was a cylindrical teat-like projection from the abdominal surface of a black terrier. The neoplasm measured 3·5 cm. × 1·8 cm. × 1·3 cm. It was of soft texture and grey-white in colour. It had the characteristic histological structure and cytological features of a mast cell neoplasm. The tissue was fixed in acid (*p*H 5·5) formalin and examined histochemically. A toluidine blue stain revealed clusters of large round cells having the characteristic metachromatic granules of mast cells (Fig. 1). The histochemical tests for 5-hydroxytryptamine have been devised to distinguish this substance from other related compounds.

Schmorl's ferric ferricyanide produced a strong reaction, indicating the presence of reducing substances in the granules which had survived formalin denaturation; catechols do not[6].

Black cytoplasmic granules in most of the mast cells of the tumour following Lillie's diazo-safranin reaction indicated the presence of enterochromaffin substance. The identity or close chemical relationship of enterochromaffin substance and 5-hydroxytryptamine is well established. Lillie claims that phenylalanine, tyrosine, tyramine, tryptophan and other tryptamines all fail to produce this reaction with this reagent[6].

Frozen sections of the material fixed in acid formalin were examined by ultra-violet light emitted from a General Electric *AH6* 1,000-watt mercury arc, and filtered through a Corning heat-absorbing blue filter and a Corning ultra-violet-transmitting filter (No. 5840) with maximum transmission at 350 mμ.

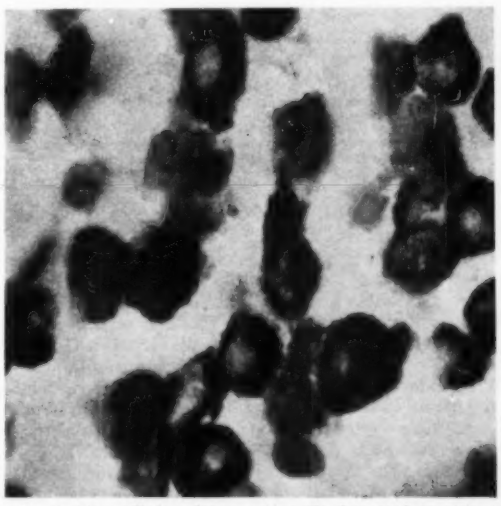

Fig. 1. Mast cells in a frozen section of a dog neoplasm stained with toluidine blue. The cytoplasmic granules which were strongly metachromatic are prominent

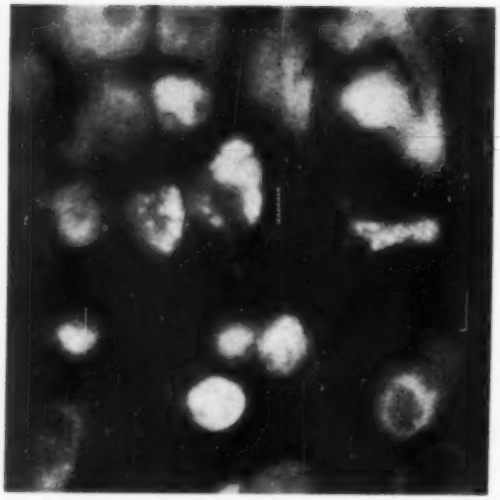

Fig. 2. Bright (orange) fluorescence in granules and in cytoplasm of the dog mast cells treated with Benditt's ninhydrin-acetic acid reaction

A Reichert Zetopan microscope equipped with an ultra-violet-transmitting dark-field condenser was used for the observations. The cytoplasmic granules of most, but not all, of the mast cells exhibited a bright golden-yellow fluorescence. The fluorescence was absent or imperceptible when a mercury arc of lower intensity (Osram 200) was used. Benditt modified Jepson and Stevens's ninhydrin method for paper chromatography[7] so that it can be used histochemically to demonstrate fluorescence of tryptamines[8]. Ninhydrin is sublimed (at 5×10^{-3} mm. mercury at 100–120° C.) on to the section of tissue which is then treated with vapours of acetic acid and acetone and examined with ultra-violet light. The mast cells so treated showed discrete, orange, fluorescent cytoplasmic globules (Fig. 2).

The following is a summary of the histochemical evidence of 5-hydroxytryptamine in the mast cell tumour :

Histochemical procedure	Results
Toluidine blue	Metachromasia of cytoplasmic granules (Fig. 1)
Schmorl's ferric ferricyanide	Strong reaction
Gomori's diazonium reaction	Strong reaction
Lillie's diazo-safranin for enterochromaffin	Strong reaction
Ultra-violet fluorescence	Golden-yellow fluorescent granules
Vapour-phase ninhydrin (for tryptamine derivatives)	Orange fluorescent granules (Fig. 2)
Methenamine-silver	Variable

According to Benditt (ref. 9 and personal communication from Benditt, E. P., to W. G. R), and Barter and Pearse[10], a specific fluorescence is produced by the interaction of acid formalin and 5-hydroxytryptamine. Catechols and resorcinol do not fluoresce like that after formalin treatment. The fluorescence noted in enterochromaffin cells after acid-formalin fixation is concluded to be due to 5-hydroxytryptamine.

This fluorescence along with positive ferric-ferricyanide and diazo-safranin (Lillie) reactions are strong presumptive evidence of the occurrence of 5-hydroxytryptamine in the mast cells of this tumour.

The variable methenamine–silver reaction cannot be equated with 5-hydroxytryptamine production[11] ; therefore, the failure consistently to reduce silver in this case does not indicate its absence.

Histochemical evidence of the presence of 5-hydroxytryptamine in a dog mast cell tumour implies an intraspecies as well as interspecies difference in its distribution in these cells. When induced ultra-violet fluorescence is being studied, the importance of using a high-intensity light source is emphasized.

This work was supported by U.S. Public Health Services research grant C-4521, and a training grant 2-G-207.

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Identification of So-called Atypical Macroglobulinæmia as an Atypical Form of β_{2A}-Paraproteinæmia : a New Immunological Entity?

Occasionally, ultracentrifugation of sera from patients with multiple myeloma yields an abnormal protein fraction with a sedimentation constant of 8–12 *S*. Jahnke and Scholtan[1] referred to such cases as "atypical macroglobulinæmia", because the sedimentation constant of these pathological proteins is smaller than that of the 'true' macroglobulins such as found in Waldenström's macroglobulinæmia.

Little is known as yet about the nature of these proteins. It was pointed out by Putnam[2] that these rapidly sedimentating proteins are exclusively encountered in the case of so-called β-myelomata. They differ from the β_{2M}-macroglobulins in immunological characteristics[3].

In sera from nine patients suffering from multiple myeloma, investigation with the aid of the ultracentrifuge revealed an abnormal protein fraction with a sedimentation constant between 8 and 12. In most cases, this rapidly sedimenting component was visible in the ultracentrifuge diagram as a sharp peak with a narrow base—a picture characteristic of paraproteinæmia.

Sulphydryl reagents did not dissociate these atypical macroglobulins into smaller 6-*S* fragments, a fact which is in contrast with the findings obtained in Waldenström's macroglobulinæmia[4]. Disulphide bridges, therefore, are probably of no importance in the macromolecular structures of the proteins under investigation.

After electrophoresis in agar-gel[5], a pathological protein fraction in the β-globulin or high-speed γ-globulin region was found in all sera (Fig. 1*a*). Two abnormal protein fractions were present in two cases. The quantitatively most important fraction was found in the β-globulin region, while the less pro-

nounced component was localized in the γ_2-globulin area (Table 1). All paraprotein fractions were periodic acid–Schiff-positive, but failed to stain with sudan black.

Two sera (*Be* and *Bu*) were examined by zone electrophoresis on starch. It was found that the paraprotein component of both sera was separated into two fractions, which could be isolated. The chemical and immunological analysis of these fractions is now in progress.

Table 1

Patient		m_r	Localization in the pherogram
Be		0·31	Between β_2 and γ-globulin
Bou		—	Dense precipitate behind application groove
Bo		0·35	Just behind the β_2-globulin
Bu		0·28	In the fast γ-globulin region
De		0·29	In the fast γ-globulin region
Le		0·29	In the fast γ-globulin region
PB	(main fraction)	0·30	Between β_2- and γ-globulin
	(small fraction)	0·12	In the slow γ-globulin region
Pa	(main fraction)	0·39	On the β_2-globulin fraction
	(small fraction)	0·27	In the fast γ-globulin region
Ve		0·41	On the β_2-globulin fraction
β_2-globulin in normal human serum		0·42	

Relative mobilities m_r of the paraprotein fractions in the serum of 9 patients with 'atypical macroglobulinæmia'. Agar-gel electrophoresis, Difco 'Nobel Agar'. Barbital buffer pH 8·6; voltage 35 V./cm. For technical details see ref. 5.

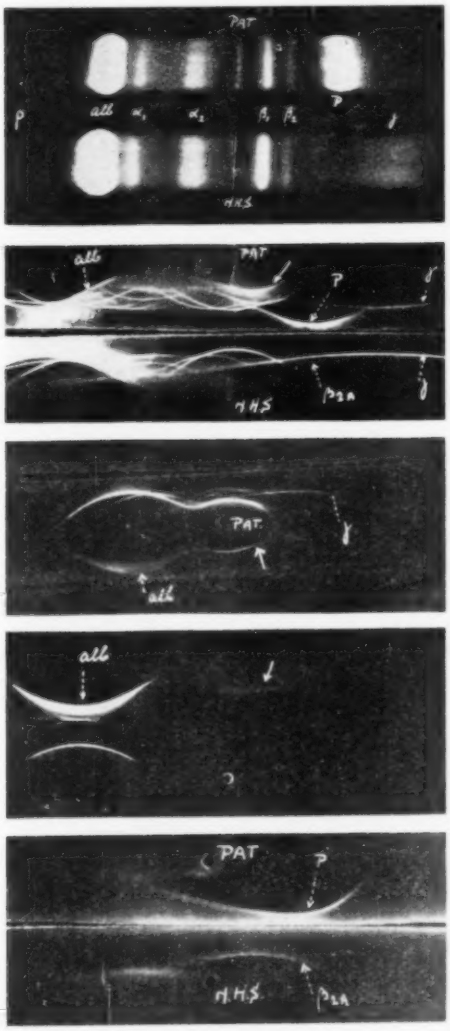

Fig. 1. *a*, Pherograms (agar gel-electrophoresis; barbital buffer pH 8·6; 35 V./cm.) obtained on normal human serum (*N.H.S.*) and on the serum of patient *Bu* (*P.47*). Note the paraprotein fraction in the latter serum (*P*). *b*, Immuno-electrophoresis of the serum of patient *Bu* (upper basin) and of normal human serum (lower basin). Note the deformation in the β_{2A}-line (*P*) and the abnormal albumin precipitation line (arrow). The antiserum used was *K*6. *c*, Immuno-electrophoresis of the serum of patient *Ve*. The antisera used were *K*6 (upper basin) and anti-human albumin immune serum (lower basin). *d*, Immuno-electrophoretic analysis of the serum of patient *Be* before (upper basin) and after (lower basin) treatment with cysteine. The antiserum used was anti-human albumin immune serum. Note the disappearance of the albumin line in the β-globulin region. *e*, Immuno-electrophoresis of the serum of patient *Bu* (upper basin) and of normal human serum (lower basin). The antiserum was *K*6, absorbed with umbilical cord serum and normal human serum. It is clearly demonstrated that the paraprotein fraction has β_{2A}-antigenic determinants

For the purpose of more precise characterization of the paraprotein fractions in the sera from our patients, these sera were submitted to immuno-electrophoretic examination. With the aid of a horse antihuman immune serum (Institut Pasteur, Paris), we obtained results such as those seen in the case of β_{2A}-myelomata[6,7]. The β_{2A}-line in the diagrams was considerably accentuated and displaced towards the antiserum reservoir (Fig. 1*b*). The β_{2M}-line was as a rule lacking. The γ-line sometimes showed shortening towards the anode side. The same results were found with a rabbit immune serum (*K*6) against the serum of one of our patients (*Be*). In the β-globulin region there was in the immuno-electrophoretic examination of all sera a short but heavy precipitation line, situated near the antigen-cup. This abnormal line, which could not be detected in immuno-electrophoretic analysis of normal human serum, shows a reaction of identity with the albumin line (Fig. 1*b*—arrow). This was clearly demonstrated by immuno-electrophoresis of the patients' sera with a rabbit anti-human albumin immune serum (Behringwerke) (Fig. 1*c*).

The abnormal protein fraction in the β-globulin region is probably a complex of albumin with a yet unknown protein. This complex could be dissociated by treatment with cysteine (Fig. 1*d*).

These findings have only been reported before by Heremans[8]. In some of the cases of β_{2A}-myeloma, investigated by him, this albumin complex in the β-globulin region was found. It is likely that these cases represent β_{2A}-paraproteinæmia with a rapidly sedimentating protein component.

Besides this abnormal albumin precipitation line there was sometimes additional abnormal precipitation lines in the β-globulin region. By immuno-electrophoresis with a rabbit anti-human γ-globulin immune serum, it was demonstrated that these lines have a γ-globulin antigenic structure.

All sera were examined by immuno-electrophoresis, with a specific rabbit anti-β_{2A}-globulin immune serum (Behringwerke) as anti-serum. In all cases, a precipitation line was visible which corresponded with the line *P* found with horse antihuman immune serum; this proved that the paraproteins under investigation did in fact possess β_{2A}-antigenic determinants.

A rabbit anti-serum (*K*6) was prepared against the serum from patient *Be*. This anti-*Be* immune serum was absorbed with umbilical cord serum and

normal human serum. After absorption, this antiserum contained only antibodies against β_2A-globulins because—both in immuno-electrophoresis with normal human serum and with the sera from our patients—it reacted by forming the β_2A-line (Fig. 1*e*). Cross-reactions were excluded with certainty because, using Ouchterlony's agar diffusion technique, reactions of identity were obtained between the sera from our patients, both with rabbit anti-β_2A-globulin immune serum and with absorbed rabbit anti-*Be* immune serum.

A β_2A-paraproteinæmia with the presence of an abnormal albumin component in the β-globulin region was found to exist in the sera from nine multiple myeloma patients examined, containing an abnormally rapid sedimenting ($s_{20} = 8 - 12$ *S*) protein fraction. If this is to be found in all cases of so-called atypical macroglobulinæmia, then it would be advisable to abandon the designation 'atypical macroglobulinæmia' (which is incorrect because it suggests a non-existing correlation with Waldenström's macroglobulinæmia[9–11]) in favour of the term 'atypical β_2A-myeloma'.

We wish to thank Dr. P. Burtin of the Institut Pasteur, Paris, for analysing two sera, and Dr. G. Schwick of the Behringwerke for supplying rabbit anti-β_2A-globulin immune serum.

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Fibrosarcoma in a Rabbit following β-Irradiation of the Skin

This communication describes the gross and histological appearance of a fibrosarcoma which occurred four years after exposing an area of rabbit skin to 16,000 rads from a phosphorus-32 plaque. The only previous observation of skin tumours in rabbits resulting from radiation exposure is contained in a recent communication by Sissons and Vaughan[1]. These workers described squamous cell carcinomas in the external auditory meatus of rabbits injected with strontium-90 at an early age. The available literature indicates a low natural incidence of tumours in rabbits[2,3].

Four years ago, we began work in this Laboratory to determine the variation in the skin reaction of rabbits, pigs and sheep after acute exposure of doses of 2,000, 8,000 and 16,000 rads of β-irradiation. Six rabbits were exposed to either strontium-90 or phosphorus-32 plaques at two sites per animal with four sites exposed to each of the dosage-levels indicated. The radiation intensity was in the range of 5,000–8,000 rads/hr. The experimental animals are being kept for their life-span. The clinical appearance of the acute and chronic reactions is being reported separately (L. A. G. and L. K. B., in preparation).

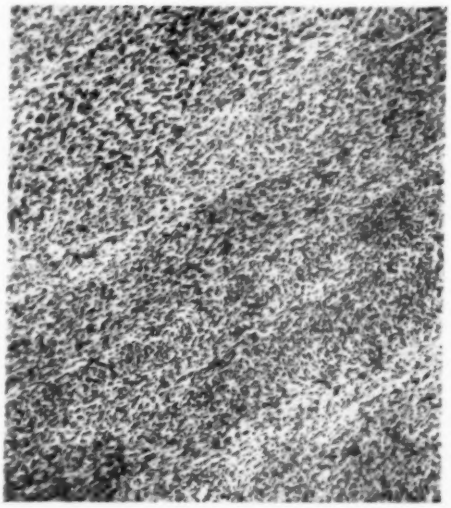

Fig. 1. Bundles of connective tissue fibres in well-differentiated areas of primary skin tumour (× 65)

The primary tumour occurred at the site of the original β-irradiation exposure. The tumour formed a moderately firm, spherical mass, measuring 6 cm. in diameter and raised to a height of 5 cm. above the body surface. The mass was located in the loose connective tissue between the body wall and the skin, which had become necrotic at the irradiation site over the tumour. Metastases were observed

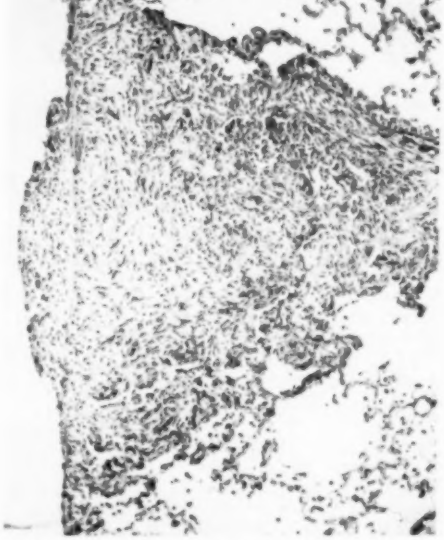

Fig. 2. Pulmonary metastasis. (× 65)

grossly in the lung. The lesions in the lungs consisted of several small (1–2 mm.), round, white nodules on the surface of the right and left diaphragmatic lobes.

The basic histological pattern of the tumour consisted of interlacing bundles of moderately cellular fibrous connective tissue (Fig. 1). The well-differentiated areas showed few mitotic figures. A network of fibres between the individual cells was demonstrated in the differentiated areas with the Laidlaw stain. Other regions of the tumour disclosed moderate pleomorphism with rounding of the nuclei and diminished formation of fibres. Mitoses were somewhat more frequent in such areas, which also contained foci of œdema and necrosis. The pulmonary metastases revealed a relatively loose pattern of fibroblastic cells (Fig. 2). The small metastases were often necrotic except for a narrow peripheral rim of viable tissue. The tumour was diagnosed pathologically as a fibrosarcoma.

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BIOLOGY

Promotion of Leaf Growth by Short Days in the Short-Day Plant *Chenopodium amaranticolor*

Past investigations into the relationship between length of day, flowering and leaf-growth have failed to explain the complex interactions between them. In most, if not all, plants the development of flower buds is associated with a reduction in leaf-growth and eventually leads to bract formation[1], and Bunning and Konder[2] have shown that leaf growth in plants maintained in a vegetative state is less for inductive than non-inductive conditions in the short- and long-day plants they studied. On the other hand some results obtained by Schwabe[3] seem on re-examination to indicate a promotion of leaf-growth by inductive conditions in *Xanthium*.

Recent work by me (the results of which will be published elsewhere) has shown that conditions leading to flowering in *Chenopodium amaranticolor* initially also promote vegetative growth. Plants which were grown from germination in 16-hr. photoperiods for 26 days were then induced to flower by transfer to various numbers of 8-hr. days. As an immediate result of such transfer the rates of leaf and axillary bud initiation at the apex increased considerably. Four days after the start of short-day treatment the daily rate of leaf initiation had increased to 3·50 from a long-day value of 0·46 and vegetative axillary bud initiation had increased from 0·46 to 2·05 a day. At the same time the rate of growth of all immature leaves was stimulated by exposure to short days, even though it was strongly

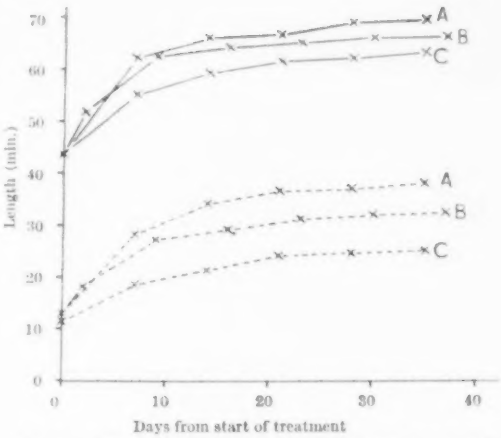

Fig. 1. Effect of inductive treatment on petiole (- - -) and lamina (——) growth of leaf 7 (8 plants per treatment). Plants were grown in long days and then received: *A*, continuous short days; *B*, two short days followed by long days; *C*, long days (control)

inhibited afterwards in induced plants. The growth of the leaf at node 7, which reached maturity before the inhibition became dominant, is shown in Fig. 1.

To test the closeness of this relationship between leaf-growth and flowering in *C. amaranticolor*, a comparison was made of the effects of short days with and without interrupted dark periods. Plants were grown in a glasshouse in continuous light (consisting of natural daylight in March–April at Palmerston North supplemented by light from 200-W. 'Sieray' mercury vapour lamps ballasted with a tungsten filament which gave an intensity of approximately 500 ft.-candles at the plant apices) for the seven weeks between germination and the start of inductive treatment. They were then divided into four groups of eight as shown in Table 1, 16 receiving 8-hr. photoperiods (−*LB*) and the other 16 receiving 7-hr. photoperiods, with 16-hr. dark periods interrupted at the mid-point by a 1-hr. light break (+*LB*) at an intensity of approximately 3,500 ft.-candles. The total amount of light received daily by each group was the same. Buds were excised from the axils of all leaves longer than 16 mm. immediately prior to short-day treatment. In 16 plants (8 + *LB*, 8 − *LB*) all apical tissue above the youngest leaf longer than 16 mm. was removed and in the other 16 the apical tissue was retained. The effect of these treatments on the growth of the youngest leaf longer than 16 mm. is shown in the table; both with and without apical tissue the growth of the − *LB* groups (flowering) was significantly higher than that of the + *LB* groups (non-flowering). It thus seems very possible that a direct relationship exists between the promotion of leaf growth and the onset of flowering. The fact that a similar relationship occurs in both the presence and absence of apices indicates that the

Table 1. Percentage Increase in Leaf Length after Six Short Days with and without Interrupted Dark Periods

	− *LB*	+ *LB*	*P* (from *t* test)
+ apex	69·14	53·75	0·019
− apex	77·40	61·25	0·044

growth stimulus is related to some step preceding the initiation of flower primordia and does not emanate from them.

Investigations to determine the universality of the promotion of leaf-growth which occurs in inductive conditions in *Chenopodium* and *Xanthium*[3] are in progress. Meanwhile the situation prevailing at the apex, where the transition to flowering is clearly associated with an increased growth-rate, indicates that such a tendency to increased leaf growth throughout the plant probably occurs very widely concomitant with the onset of flowering. Once flower primordia are formed, however, they exert a strong inhibitory influence on leaf growth which quickly suppresses any initial stimulation which might have been present.

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Estimation of Oil in Safflower Seed

Weight per measured bushel is a widely used index of physical quality of grain[1]. In applying this measure of quality to varieties of safflower (*Carthamus tinctorius*) grown on dry land in southern Alberta during 1957–60, there was a correlation of $r = -0.68$ ($P < 0.01$) between oil percentage and bushel weight. The weight per measured bushel of varieties varied from 36·5 to 49·5 lb., whereas the oil content varied from 37·9 to 25·0 per cent, respectively. Since this relationship is contrary to that generally expected, some of the physical and chemical properties of the seed were investigated. Seed from fourteen varieties grown at three locations were used for this purpose.

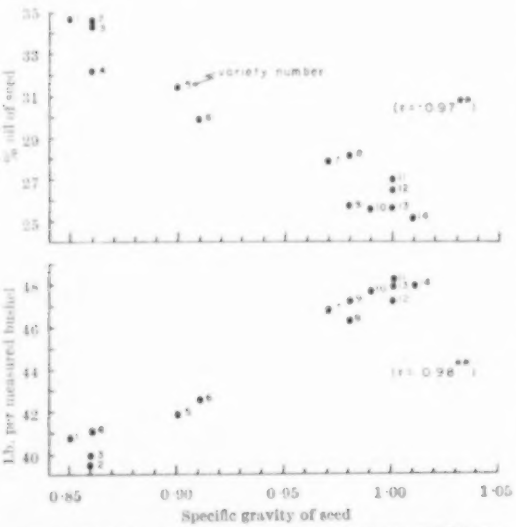

Fig. 1. The interrelationship between oil percentage, weight per measured bushel, and specific gravity of the seed of 14 safflower varieties. $P < 0.01$

The specific gravity of the seed was determined for each variety on the basis of four 100-seed samples from each location. The varietal means for three locations for oil percentage, specific gravity, and bushel weight are shown in Fig. 1. It is evident from these results (Fig. 1) that varieties with low oil percentages could be eliminated on the basis of either their high bushel weight or high specific gravity. This relationship between oil percentage and specific gravity of seed is sufficiently close to be of practical value in evaluating safflower lines for their oil content. The weight per measured bushel is easily obtained where a substantial quantity of seed is available, but the specific gravity index has the advantage of being equally applicable to both small and large quantities of seed. Furthermore, it can be used to advantage in screening segregating populations.

Since low specific gravity of seed is associated with high oil percentage, additional analyses were carried out to determine some of the factors that might contribute to this relationship. The percentage air space inside the seed was calculated for each variety by determining the difference in volume between whole and split seed. The hull with adhering seed coat was separated from the kernel to calculate the percentage hull of the seed and percentage oil in the kernel. Varietal means of three locations for these determinations are given in Fig. 2. The percentage air space inside the seed and oil percentage of the kernel decreased with increasing specific gravity whereas the hull percentage increased. The association between specific gravity of seed and hull percentage was investigated further by determining the

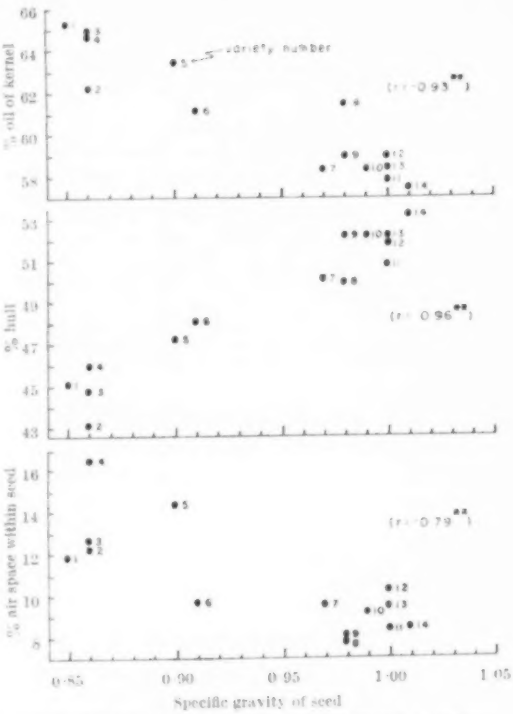

Fig. 2. The interrelationship between specific gravity of safflower seed, air space inside the seed, oil percentage of kernels, and hull percentage. $P < 0.01$

specific gravity of the hulls. Although the specific gravity of the hull was found to vary with varieties, it was always greater than that of the whole seed. This explains the close relationship between specific gravity of seed and percentage hull. The high specific gravity of hull and the factors illustrated in Fig. 2 clarify the relationship between high oil percentage and low specific gravity of safflower seeds.

These results will be reported in greater detail elsewhere.

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Potato Root Eelworm in the Canary Islands

The European and Mediterranean Plant Protection Organisation annual reports 1953–1959, which survey the incidence of the potato root eelworm, *Heterodera rostochiensis*, record the occurrence of this major pest of potatoes in all member countries except Italy, Yugoslavia, Rumania, Turkey, Cyprus, Malta, Libya and Tunisia.

On December 27, 1960, in company with Sr. Iuan Valladares Barbuxano, Ingeniero Agronomo de la Jefatura Agronomica, I discovered the existence of *H. rostochiensis* in potato fields at La Victoria de Acentejo and in other districts in the north of Tenerife, Canary Islands. At latitude 28° 25′ N., this would appear to be the most southerly occurrence as yet recorded in the geographical distribution of *H. rostochiensis* in the Old World.

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A Technique for Destruction of the Pineal Body using Yttrium-90 Spheres

Excision of the pineal body, first described by Exner and Boerse[1], has been frequently used in the study of pineal function and has been performed in various groups of animals[2]. Thermocauterization and stereotaxic ablation have also been employed. The operative mortality with the latter methods has been quite high due to haemorrhage from adjacent blood vessels[2].

A technique using yttrium-90 spheres for radiological destruction of the pituitary gland was recently introduced[3]. The same source of radiation was used in the present work. The yttrium spheres were manufactured as described by Ginell and Simon[4] and by Ginell and Doering[5]. The activity of the spheres following activation in an atomic reactor was calculated as described by Notter and by Notter *et al.*[3,6]. A 2–3 cm. mid-line incision was made over the occipital region of fifteen rats following anæsthesia which was maintained with ether. A hole about 1·5 cm. in diameter was drilled exactly above the site of the pineal body. The position of the hole had been calculated in relation to the visible sutures between the parietalia and the occipital bone (checked by X-ray photograph, Fig. 1). Three or

Fig. 1. X-ray photograph of the skull showing the site of the spheres. (× 3)

four spheres were inserted on and around the pineal body. Damage to the venous sinuses, which overlie the gland, could not be avoided but the bleeding induced was easily stopped.

Four experimental animals died within 2–4 days following the operation, whereas the remaining survived and were killed on the 15th, 20th and 35th day after the operation. The brains and endocrine organs were then fixed for future examination. A preliminary examination of the irradiated tissue of the pineal brain region showed complete necrosis of the pineal body in eight cases. The radiation dose needed to obtain complete necrosis, provided that the spheres were placed correctly in relation to the pineal body, was calculated as approximately 100,000 −150,000 rads, thus causing necrosis at the distance of 1·5–2 mm. from the periphery of the spheres.

No appreciable radiation damage was found in the cortex of the brain adjacent to the pineal body.

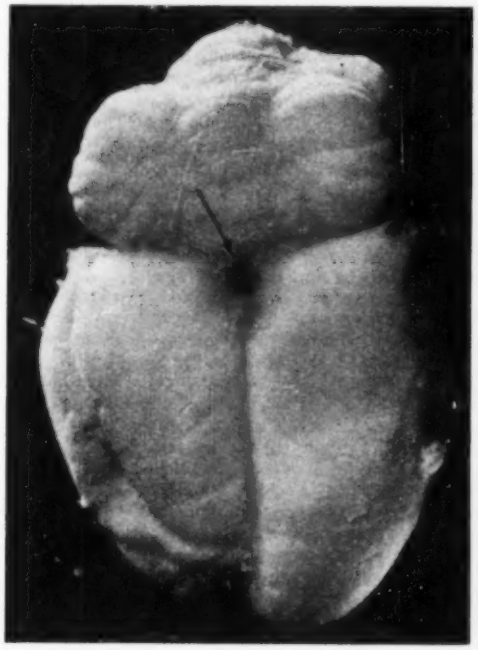

Fig. 2. Dorsal view of the rat brain indicating the position of one of the yttrium spheres. (× 3)

except for two cases in which the spheres had been placed incorrectly in relation to the pineal body. Partial necrosis of the pineal body (50–80 per cent) was obtained in a few cases in which the position of the spheres apparently had not been optimal in relation to the pineal body. However, since a total of eight cases out of 11 surviving cases were obtained with a complete destruction of the pineal body, it was concluded that the method described must be considered as a suitable means for localized destruction of the pineal body, and other small tissue areas as well.

This work was supported in part by the Tullberg Fund, University of Uppsala. We acknowledge the advice of Prof. M. D. Altschule, McLean's Hospital, Waverley, Mass., in preparing the manuscript.

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A Biennial Copepod from Lake Hazen, Ellesmere Island

Several species of copepods in the Arctic are known to have annual life-cycles in the sea[1] and freshwater[2], and macroplanktonic Crustacea of northern seas may not breed until two years old[3]. So far as I am aware, no copepod has been described with a life-cycle greater than one year, and the extreme response of *Cyclops scutifer* in Lake Hazen to conditions of low temperature and limited food seems worth recording.

Lake Hazen (lat. 81° 45′ N., long. 71° 00′ W.) is the largest lake of the Queen Elizabeth Islands of high-arctic Canada. It is glacier-fed, cold and deep, and is not always entirely free from ice in summer. Primary productivity is very low, and the fauna is small in species and individuals.

The zooplankton was sampled regularly between mid-June and mid-August. The proportions of naupliar and copepodite stages at one offshore station on four successive dates are given in Fig. 1. The proportions of the stages were very similar in plankton collections from other parts of the Lake. The conspicuous and persistent bimodality of the population throughout the short sampling period can only be the result of a basically biennial life-history. A very few adults were taken in a surface haul on August 11, the last date of sampling, but presumably most copepodites do not reach adult-hood and breed until the autumn months. The products of this breeding pass the winter as nauplii and just begin to enter the copepodite stages by the following summer. The possibility of slight exchange between the generations is suggested by the stage I copepodites of June 18 and the stage II copepodites of August 11.

Fig. 1. The proportions of the stages of nauplii and copepodites of *Cyclops scutifer* in vertical plankton hauls from 32 m. at the same station on four successive dates. No adults (CVI) were taken in the vertical haul of August 11, but a few were taken in a nearby surface collection on that date

I am indebted to Dr. Edward B. Reed, Colorado State University, for finding the half-dozen adult copepods in the entire collection and identifying the species as *Cyclops scutifer* Sars. Field work was carried out in summer 1958 on the Canadian International Geophysical Year expedition to Ellesmere Island, organized by the Defence Research Board of Canada. Collections were analysed at the Bingham Oceanographic Laboratory, Yale University. A more complete account of the aquatic biology of Lake Hazen is in preparation.

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BACTERIOLOGY

Biosynthesis of Acetoin by *Leuconostoc citrovorum*

It has been shown[1] that in most bacterial cells acetoin is formed by the condensation of pyruvate and activated acetaldehyde. The findings of Beckhorn[2], De Man[3] and Mizuno and Jezeski[4] leave no doubt that in the heterofermentative genus *Leuconostoc* the synthesis occurs via acetolactate. It is still uncertain, however, if acetoin is formed from sugar and, if so, out of which part of the carbon chain of the sugar. Preliminary experiments showed that washed cell suspensions of *Leuconostoc citrovorum* ATCC 8082 do not form acetoin during glucose fermentation in a phosphate buffer. On the other hand, a large amount of acetoin is produced from pyruvate. When pyruvate and glucose are added simultaneously, the synthesis of acetoin is inhibited.

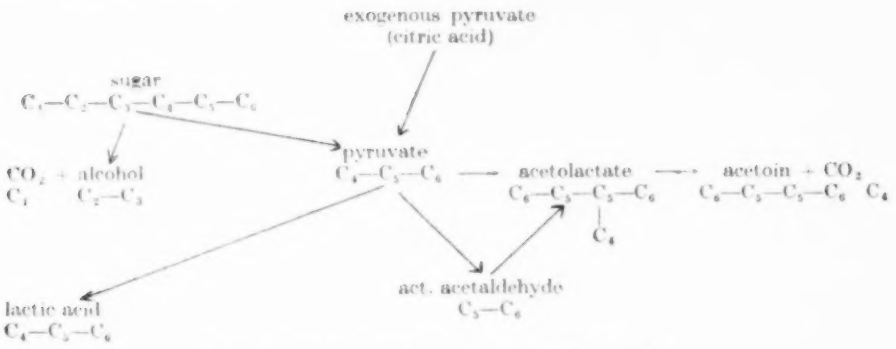

Fig. 1. Scheme of acetoin synthesis by *Leuconostoc citrovorum*

Only at the end of the fermentation, when the glucose concentration becomes so low that the production of carbon dioxide decreases, does the synthesis of acetoin begin. In the presence of a favourable H-donator (glucose) the pyruvate in the cell is presumably reduced so quickly to lactic acid that the condensation of pyruvate to acetolactate does not occur.

In order to check if any part of the carbon skeleton of glucose is actually used for the synthesis of acetoin, glucose-1-^{14}C, 2-^{14}C and 6-^{14}C were fermented with aliquot parts of a *Leuconostoc* suspension in the presence of a 5-fold excess of pyruvate. After the drop in carbon dioxide production the radioactivity in the acetoin formed was determined. As shown in Table 1, radioactive acetoin is produced only when glucose-6-^{14}C is employed. The specific activity was eight times less than that of the corresponding carbon atoms in the glucose. From this one may conclude that only one-eighth of the synthesized acetoin results from the carbon chain of glucose, the rest from pyruvate. In addition it is seen from Table 1 that only the lower part of glucose can be used for the synthesis of acetoin, and not the $C_{2,3}$ moiety, which appears as alcohol during fermentation. According to the results of Heath *et al.*[5], $C_{2,3}$ first yields acetylphosphate, which is probably reduced further to alcohol via acetaldehyde. Obviously the acetaldehyde cannot be activated and is not used for the synthesis of acetoin. Thus the scheme presented in Fig. 1 may be considered as established for the formation of acetoin in the heterofermentative genus *Leuconostoc*.

In contrast to these findings, Andersen[6] reported recently that *Leuconostoc citrovorum* ATCC 8081 may produce radioactive acetoin from glucose-1-^{14}C as well as from glucose-6-^{14}C, thus behaving like the homofermentative *Str. diacetilactis*. This result may be explained by the observation of Felton and Niven[7] that the mentioned strain ATCC 8081 is not *Leuconostoc citrovorum* but the homofermentative *Pediococcus cerevisiae*. To demonstrate clearly that our strain represents a heterofermentative *Leuconostoc*, the radioactivity in the fermentation products of spot-labelled glucose was determined. The result obtained is identical with that of Gibbs *et al.*[8]. A more detailed account will be published in *Zentralbl. f. Bakt.*

Table 1. Specific Activity of Acetoin after Fermentation of Labelled Glucose in the Presence of Unlabelled Pyruvate

	Barium carbonate (mgm.)	Specific activity (mμc./mM acetoin)
Glucose-1-^{14}C	10·72	0·64
Glucose-2-^{14}C	11·78	0·77
Glucose-6-^{14}C	10·57	32·30

Pyruvate, 500 μM; glucose, 100 μM; manganese chloride, 8 mgm.; calcium chloride, 8 mgm.; phosphate buffer, 0·1 N; pH 4·8. Total volume, 20 ml.; glucose-1-^{14}C, 89·2 mμc./mM; glucose-2-^{14}C, 77·3 mμc./mM; glucose-6-^{14}C, 81·0 mμc./mM.

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Chloramphenicol, a Simultaneous Carbon and Nitrogen Source for a *Streptomyces* sp. from Egyptian Soil

In work concerning the decomposition of antibiotics in soil and micro-organisms capable of this process, a chloramphenicol solution (250 μgm. chloramphenicol/gm. soil) was percolated through 25-gm. sieved fresh garden soil, pH 7·5, in an apparatus similar to that described by Lees and Quastel[1]. The chloramphenicol was applied in three doses; the first dissolved in 50 ml. sterile distilled water and the others in 5 ml. added to the percolate in the reservoir. The antibiotic was bioassayed daily against *Bacillus subtilis*. The first dose disappeared after 11 days and the second and third after 3 days.

Isolation of the micro-organisms involved in the decomposition of chloramphenicol was then carried out by plating the enriched soil in a medium containing the antibiotic as the sole organic carbon source. The medium (ammonium nitrate chloramphenicol medium) contained, in gm. per 100 ml., crystalline magnesium sulphate, 0·5; crystalline ferrous sulphate, 0·003; calcium chloride, 0·005; potassium dihydrogen phosphate, 0·1; dipotassium hydrogen phosphate, 0·25; ammonium nitrate, 0·05; agar, 1·3—adjusted to pH 7·0–7·2, dispensed in 100 ml. quan-

tities and autoclaved at 15 lb. for 15 min. Before use, the medium was melted, cooled to 50° C. and chloramphenicol (100 μgm./ml.) added. Plates were incubated at 30° C. for 15 days. Only one type of organism appeared on the plates of the highest dilution (10^{-5}), a *Streptomyces* producing greyish-white thin mycelium and chains of chalky white rod-shaped conidia ($1{\cdot}6 \times 0{\cdot}8\mu$ in stained preparations) borne on long open-spiral conidiophores (section *Spira* in the classification of Pridham, Hesseltine and Benedict[2]). Its cultural characteristics on the media proposed by Waksman[3] were: mycelium greyish-white on Czapek's and starch agar and nutrient gelatin, orange on glucose asparagine, glycerol asparagine and yeast glucose agar media, and lemon-yellow on nutrient agar. Chalky white conidia were produced on all the media except on nutrient gelatin where the growth was markedly poor. Pigmentation of the mycelium appeared to be connected with the heaviness of growth; on media showing non-pigmented mycelia the growth was poorer than that produced on media that revealed pigmentation. Growth in liquid media was restricted to a thin unpigmented pellicle consisting of more or less separate colonies which acquired a chalky white surface when conidia were formed. None of the media tested induced the formation of diffusible pigments. Glucose, saccharose, lactose and mannitol were not utilized. There was no hydrolysis of starch, liquefaction of gelatin, digestion of casein or cellulose, production of ammonia from peptone or reduction of nitrate. Litmus milk turned alkaline after 15 days. Growth took place at 18° and 30° but not at 55° C. The organism resisted pasteurization in glucose broth at 60° C. for 30 min. It had no antagonistic properties when tested against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Mycobacterium phlei*.

Repeated sub-culture (6 times) in the ammonium nitrate chloramphenicol liquid medium, using straight wire inoculation, always resulted in growth accompanied by the inactivation of the antibiotic, that is, the organism is capable of utilizing chloramphenicol as the sole source of carbon. On sub-culturing in the same manner (6 times) in the liquid medium without ammonium nitrate (chloramphenicol medium) growth and inactivation of the antibiotic again occurred, that is, the organism is capable of utilizing chloramphenicol also as the sole source of nitrogen. This property was confirmed when the growth in the chloramphenicol medium was centrifuged, twice washed with sterile distilled water and used for inoculating fresh media (Table 1). Repeated sub-culturing decreased the inactivation period and improved growth. Inoculation of the liquid medium without chloramphenicol failed to produce visible growth after periods of incubation up to one month.

Table 1. Disappearance of Chloramphenicol on Repeated Sub-culturing with Washed *Streptomyces*, Incubation at 30° C.

	100 μgm./ml.*		250 μgm./ml.*	
	Inactivation period (days)	Visible growth†	Inactivation period (days)	Visible growth†
First sub-culture	7	+	20	+
Second ,,	3	++	7	++
Third ,,	3	++	5	++
Fourth ,,	−	−	2	+++

* In non-inoculated controls the variation in diameter of inhibition zones did not exceed ± 0·5 mm. in 20 days incubation.
† Seven days growth on glucose broth ++++.

The ability of the organism to grow in increasing concentrations of chloramphenicol as sole carbon and nitrogen source was tested by inoculating 100 ml. quantities of medium containing 100, 250, 350, 400, 500, 550, 600 and 1,000 μgm. chloramphenicol ml. with a loopful of 7-day culture in chloramphenicol liquid medium (100 μgm./ml.). Growth of the organism and inactivation of the antibiotic took place in all concentrations up to 600 μgm./ml., where the antibiotic completely disappeared after 13 days. No growth or reduction in activity could be detected within one month in the medium containing 1,000 μgm./ml.

Finally, the purity of the *l*-chloramphenicol used (Kemicetine, Carlo Erba) was verified by the determination of its melting point, carbon, nitrogen, hydrogen and chloride contents and by checking the weight in the capsules supplied.

Work is in progress to elucidate the mechanism of the decomposition of chloramphenicol by the isolate.

We wish to express our thanks to Dr. T. Gibson of the School of Agriculture, Edinburgh, for constructive criticism.

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PSYCHOLOGY

An Unexpected Effect of Attention in Peripheral Vision

The phenomenon described here suggests an unexpected effect of attention in peripheral vision.

Arrange a number of small objects such as keys, coins, etc., on a table and fixate a point among them from some convenient distance, say 3 ft. Maintaining fixation of the point selected, attend to one of the objects and try to see or describe it in detail.

A number of people including experienced psychologists and physiologists have carried out this procedure and have reported what I had previously found, namely, that the object selected for attention becomes hazy and may even disappear. The effect may persist for seconds at a time or it may be fleeting or fluctuating; but other objects in the field remain steadily visible meantime.

It is well known that the whole visual field may disappear when it is 'stabilized', and some people report that this occurs with steady fixation.

The blurring or disappearance of small regions selected for deliberate attention is, however, a different matter and suggests some form of central interference.

Much remains to be done in determining limiting conditions for the occurrence of the phenomenon and in discovering whether it is affected by training and practice. It is in any event a striking example of attention being associated with a loss rather than a gain in clarity.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, March 6

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 5 p.m.—Mr. Stanislaw Leszczycki (Geographical Institute of the Polish Academy of Sciences): "The Economic Regions of Poland".

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. E. D. R. Shearman: "An Investigation on the Usefulness of Back-Scatter Sounding in the Operation of H.F. Broadcasting Services".

SOCIETY OF ENGINEERS (at the GEOLOGICAL SOCIETY, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. H. Kaylor: "Some Aspects of Pre-stressed Concrete".

UNIVERSITY OF LONDON (at Bedford College, Inner Circle, Regent's Park, London, N.W.1), at 5.30 p.m.—Prof. E. Wegmann (Neuchâtel): "Some Aspects of the Geology of the Basements".*

UNIVERSITY OF LONDON (in the Eugenics Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.45 p.m.—Prof. Harald Cramér (Sweden): "Some Recent Results in the Theory and Applications of Stochastic Processes".* (Further lectures on March 10 and 13.)

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Mr. M. J. Langford: "Photography in Industry and Commerce" (Cantor Lecture).

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. A. Dahlén (Sweden): "Chemical Industry in Sweden".

SOCIETY FOR VISITING SCIENTISTS (at 5 Old Burlington Street, London, W.1), at 7.30 p.m.—Discussion Meeting on "Scientific Methods in Archæology". Chairman: Dr. E. T. Hall. Speakers: Dr. C. M. Lerici, Mr. M. J. Aitken and Dr. E. H. Willis.

Monday, March 6—Thursday, March 9

OIL AND COLOUR CHEMISTS' ASSOCIATION (in the Royal Horticultural Society's New Hall, Westminster, London, S.W.1)—Thirteenth Technical Exhibition.*

Tuesday, March 7

INSTITUTION OF CHEMICAL ENGINEERS (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 4 p.m.—Papers on: "Fluidization".

UNIVERSITY OF LONDON (at the London School of Economics and Political Science, Houghton Street, London, W.C.2), at 5 p.m.—Prof. Eric Voegelin: "World Empire and the Unity of Mankind" (Stevenson Memorial Lecture).*

ROYAL SOCIETY OF ARTS, COMMONWEALTH SECTION (at John Adam Street, Adelphi, London, W.C.2), at 5.15 p.m.—Sir John Macpherson, G.C.M.G.: "Sovereign Nigeria".

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND CONTROL SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. A. V. Hemingway and Mr. R. L. Dressler: "The Automatic Control of Machines for Assembling Mechanical Components".

UNIVERSITY OF LONDON (at Bedford College, Inner Circle, Regent's Park, London, N.W.1), at 5.30 p.m.—Prof. E. Wegmann (Neuchâtel): "The Folded Chain of the Jura Mountains".*

UNIVERSITY OF LONDON (at Imperial College of Science and Technology, Prince Consort Road, London, S.W.7), at 5.30 p.m.—Dr. C. G. Wynne: "The Correction of Aberration in Optical Systems".

UNIVERSITY OF LONDON (at King's College, Strand, London, W.C.2), at 5.30 p.m.—Prof. H. Lundegårdh (Sweden): "Electron Transport Mechanisms in Plant Cells".* (Further lecture on March 8.)

UNIVERSITY OF LONDON (at the School of Pharmacy, 29–39 Brunswick Square, London, W.C.1), at 5.30 p.m.—Prof. H. W. Mossman (University of Wisconsin): "Glandular Tissues of the Mammalian Ovary".*

UNIVERSITY OF LONDON (in the Gustave Tuck Theatre, Univetsity College, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. D. T. Swift-Hook: "Magnetohydrodynamic Generation".* (Third of five lectures on "Generation of Electricity without the use of Rotating Machinery".)

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at Hatfield Technical College, Roe Green, Hatfield, Herts), at 7.30 p.m.—Mr. D. Hurden: "Some Chemical Problems of Space Flight".

Wednesday, March 8

ZOOLOGICAL SOCIETY OF LONDON (in the Meeting Room of the Zoological Society, Regent's Park, London, N.W.1), at 10.30 a.m.—Symposium on "Aspects of Disease Transmission by Ticks".

INSTITUTION OF MECHANICAL ENGINEERS, INTERNAL COMBUSTION ENGINE GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 3 p.m.—Meeting on "The Mechanics of the Formation and Adhesion of Deposits Arising from the Combustion of Liquid Fuel".

PALÆONTOLOGICAL ASSOCIATION (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Annual General Meeting. Prof. T. M. Harris: "The Fossil Cycads" (Fourth Annual Address).

UNIVERSITY OF LONDON (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. K. Kramer (University of Göttingen): "Renal Blood Flow in Relation to the Counter Current System".*

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Sir Andrew McCance, F.R.S.: "The Steel Industry To-day and To-morrow".

ROYAL INSTITUTE OF CHEMISTRY (joint meeting with the CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY CHEMICAL SOCIETY, at the Chelsea College of Science and Technology, Manresa Road, London, S.W.3), at 7 p.m.—Prof. G. A. D. Haslewood: "Newer Chemistry of Bile Acids and Alcohols".

Thursday, March 9

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. D. P. Craig, Mr. J. M. Hollas, Mr. M. F. Redies and Mr. S. C. Wait: "Analysis of the Naphthalene Vapour Absorption Bands at 3200 Å. I: Naphthalene *h*-*s*. II: Naphthalene *d*-*s*".

Friday, March 10

ASSOCIATION OF APPLIED BIOLOGISTS (at Rothamsted Manor, Harpenden, Herts), at 10.50 a.m.—Meeting on "Aspects of Crop Physiology".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. Ronald King: "Energy".

Saturday, March 11

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London, S.E.23), at 3.30 p.m.—Mr. C. M. Mitchell: "The Folk Life of the English People".*

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

BIOCHEMIST for the Wellcome Laboratory, situated at the Veterinary Hospital—The Secretary of the University Court, The University, Glasgow, W.2 (March 10).

JUNIOR RESEARCH FELLOW IN CHEMISTRY—The College Secretary, Balliol College, Oxford (March 11).

LECTURER, and an ASSISTANT LECTURER, IN BOTANY; an ASSISTANT LECTURER IN CHEMISTRY; an ASSISTANT LECTURER IN PHYSIOLOGY; and an ASSISTANT LECTURER IN ZOOLOGY—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8 (March 11).

LECTURER IN APPLIED MECHANICS—The Registrar, The University, Leicester (March 11).

RESEARCH ASSISTANT (BIOLOGIST or CHEMIST) at Poole, Dorset, to assist in research on the tank culture of bivalve shellfish, under the supervision of the professor of zoology, University of Southampton—The Secretary and Registrar, The University, Southampton (March 11).

RESEARCH ASSISTANT (non-medical or medical graduate), to study wound healing by light and electron microscopy—Prof. R. J. Harrison, Anatomy Department, The London Hospital Medical College, Turner Street, London, E.1 (March 11).

ASSISTANT LECTURER IN PHILOSOPHY; and an ASSISTANT LECTURER IN MORAL AND POLITICAL PHILOSOPHY—The Registrar, University College of North Staffordshire, Keele, Staffs (March 14).

RESEARCH ASSISTANT (preferably with experience or an interest in comparative endocrinology or histochemistry) IN THE DEPARTMENT OF ZOOLOGY—The Registrar, The University, Nottingham (March 18).

RESEARCH STUDENTS (2) (suitably qualified in zoology, biochemistry or pharmacology) in the Wellcome Laboratories of Pharmacology, the Gatty Marine Laboratory, St. Andrews, for work on thyroid metabolism and physiology of lower vertebrates—Joint Clerk to the University Court, College Gate, St. Andrews (March 18).

LECTURER and an ASSISTANT LECTURER IN PURE MATHEMATICS—Dr. F. G. Friedlander, Secretary of the Appointments Committee of the Faculty of Mathematics, The University, Arts School, Bene't Street, Cambridge (March 22).

ASSISTANT LECTURER (trained in electron microscopic techniques) IN BIOPHYSICS—The Registrar, The University, Manchester 13 (March 25).

LECTURER IN CHEMISTRY (INORGANIC)—The Secretary, The University, Aberdeen (March 25).

LECTURER or ASSISTANT LECTURER (qualified in pure or applied mathematics) IN MATHEMATICS—The Registrar, University College of North Staffordshire, Keele, Staffs (March 25).

PROFESSOR (with a higher degree, preferably a doctorate, and with research experience in the field of animal husbandry) OF ANIMAL HUSBANDRY within the Faculty of Veterinary Science, University of Queensland—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, April 15).

COMPUTER OFFICER IN THE SUB-DEPARTMENT OF NUMERICAL ANALYSIS—The Registrar, The University, Liverpool, quoting Ref. No. CV/T.

DISTILLERS COMPANY RESEARCH STUDENT IN THE DEPARTMENT OF CHEMICAL ENGINEERING, for work leading to a higher degree on the kinetics of the gaseous oxidation of aromatic hydrocarbons—The Secretary, University College, Gower Street, London, W.C.1.

HEAD OF THE DEPARTMENT OF SCIENCE, Grade II—The Principal, Loughborough College of Further Education, Greenclose Lane, Loughborough.

POST-DOCTORAL FELLOW IN THE CHEMISTRY OF THIOAROMATIC COMPOUNDS IN ACID SOLUTIONS; the research will involve organic chemistry and electron spin resonance spectroscopy—Prof. H. J. Shine, Texas Technological College, Lubbock, Texas, U.S.A.

SCIENTIFIC OFFICER (male or female, with an honours degree in science, pharmacy or biology), for duties consisting of technical work

in the Blood Transfusion Service Laboratories—The Director, Blood Transfusion Service, Roby Street, Manchester 1.

SCIENTIFIC OFFICER (with a good honours degree in biochemistry or chemistry and with a particular interest in lipid metabolism), to investigate the interrelationship between sterol and fatty acid metabolism in animals—The Secretary, National Institute for Research in Dairying, Shinfield, Reading, quoting Ref. 617.

SENIOR LECTURER (with an honours degree and suitable teaching and research experience, and preferably higher degrees and specialization in modern atomic physics) IN PHYSICS—The Clerk to the Governors, South-West Essex Technical College and School of Art, Forest Road, Walthamstow, London, E.17.

SENIOR TECHNICIAN (preferably with G.C.E. ("A") level in either biology or zoology) IN THE ZOOLOGY DEPARTMENT, to assist in research of Prof. P. B. Medawar and his group on transplantation—The Secretary, University College, Gower Street, London, W.C.1, quoting "Zoology/1".

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The Species Unit, and Archetypal, Primeval and Primitive Vegetation. By Marietta Pallis. Pp. 20. (Glasgow: Robert Maclehose and Co., Ltd., 1960.) [2411

The Mersey Docks and Harbour Board. Annual Review for the year ended 1st July, 1960. Pp. 16. (Liverpool: Mersey Docks and Harbour Board, 1960.) [2411

Geology and the History of Life. By Prof. P. C. Sylvester-Bradley. (An inaugural lecture delivered at the University, Leicester, 9 February, 1960.) Pp. 27. (Leicester: Leicester University Press, 1960.) 5*s*. [2411

A Guide to Information on Atomic Energy in Britain: a Selected List of British Books, Periodicals, Reports, Films, Photographs and Display Materials describing the latest developments in the United Kingdom. (Prepared by the Central Office of Information, with the co-operation of the United Kingdom Atomic Energy Authority.) Pp. 64. (London: H.M. Stationery Office, 1960.) 5*s*. net. [2811

Ciba (A.R.L.), Limited, Technical Notes, No. 215 (November 1960): Glued Acoustic Partitions. Pp. 6. (Duxford: Ciba (A.R.L.), Limited, 1960.) [2811

Some Problems of Human Geography: an Inaugural Lecture. By Prof. Robert E. Dickinson. Pp. ii + 36. (Leeds: The University Press, 1960.) 2*s*. 6*d*. [2811

The British Society for International Understanding. Annual Report for 1960. Pp. 10. (London: The British Society for International Understanding, 1960.) [2911

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 702, Vol. 243 (24 November 1960): Lampbrush Chromosomes of Crested Newts *Triturus cristatus* (Laurenti). By H. G. Callan and L. Lloyd. Pp. 135–219 + plates 17–25. (London: The Royal Society, 1960.) 42*s*. [2911

Institution of Electrical Engineers. List of Members. Part 2: Associates, Graduates and Students. Pp. 428 + 36A. Supplement to List of Members, Part 1: Corporate Members and Companions. Pp. 8. (London: Institution of Electrical Engineers, 1960.) [3011

Aslib Cranfield Research Project: Interim Report on the Test Programme of an Investigation into the Comparative Efficiency of Indexing Systems. By Cyril W. Cleverdon. (An investigation supported by a grant to Aslib by the National Science Foundation.) Pp. iii + 84. (Cranfield: College of Aeronautics, 1960.) 8*s*. 6*d*. [3011

Bulletin of the British Museum (Natural History). Botany. Vol. 2, No. 9: *Saxifraga* of the Himalaya. 2: Some New Species. By Harry Smith. Pp. 227–260 + plates 13–21. (London: British Museum (Natural History), 1960.) 21*s*. [112

Air Ministry: Meteorological Office. Geophysical Memoirs, No. 103: Upper Winds Over the World, Parts 1 and 2. By H. Heastie and P. M. Stephenson. Pp. i + 217. (M.O. 631c.) (London: H.M. Stationery Office, 1960.) 30*s*. net. [112

Population Density Map, 1951. Compiled by the Ministry of Housing and Local Government from the County Reports of the 1951 Census. (Ordnance Survey "Ten Mile" Map of Great Britain, Sheet 2.) (Chessington: Ordnance Survey, 1960.) 5*s*. net. [112

Other Countries

Yale Peabody Museum of Natural History. Postilla, No. 39 (May 2, 1959): On *Makaira nigricans* of Lacépède. By James E. Morrow, Jr. Pp. 12. No. 40 (May 28, 1959): A New Species of *Grammatostomias* (Family Melanostomiatidae) from the Western North Atlantic. By James E. Morrow, Jr. Pp. 4. No. 44 (February 15, 1960): *Sinops* from the Cuchara Formation of Colorado. By Peter Robinson. Pp. 4. No. 46 (June 30, 1960): Additions to the Avifauna of Northern Angola, 1. By S. Dillon Ripley and G. H. Heinrich. Pp. 7. Bulletin No. 15: Stratigraphy and Micropaleontology of the Thermapolis Shale. By Don L. Eicher. Pp. iv + 126 + 6 plates. Annual Report, 1960. Pp. 31. (New Haven, Conn.: Peabody Museum of Natural History, Yale University, 1959 and 1960.) [2411

Centro Brasileiro de Pesquisas Fisicas. Rio de Janeiro. Notas de Fisica. Vol. 6, No. 5: Photon Decay of Hyperons. By Prem Prakash and A. H. Zimerman. Pp. 139–163. Vol. 6, No. 6: The Penetration of a Wave Into a Potential Barrier. By Guido Beck. Pp. 165–173. Vol. 6, No. 7: An Investigation of some (3He,d) Reactions in Light Nuclei at 5.2 Mev. By P. D. Forsyth, A. A. Jaffe, I. J. Taylor, S. Ramavataram and F. de S. Barros. Pp. 175–200. (Rio de Janeiro: Centro Brasileiro de Pesquisas Fisicas, 1960.) [2411

Indian Forest Bulletin No. 203 (Minor Forest Products), (New Series): Indian Woods Tested for Match Manufacture. By A. C. Dey and S. Ramaswami. Pp. i + 41. (Delhi: Manager of Publications, 1960.) Rs. 2.37nP.; 4*s*. [2411

The Natural History of Rennell Island, British Solomon Islands. Vol. 3: (Botany and Geology). Scientific Results of the Danish Rennell Expedition, 1951, and the British Museum (Natural History) Expedition, 1953. Pp. 132 + 10 plates. (Copenhagen: Danish Science Press, Ltd., 1960.) 30 D.kr. [2411

Canada: Department of Northern Affairs and National Resources. Bulletin No. 163 (Anthropological Series, No. 46): Indian Days on the Western Prairies. By Marius Barbeau. Pp. vi + 234 (165 plates). 4 dollars. Bulletin No. 165 (Anthropological Series No. 47): Huron-Wyandot Traditional Narratives, in Translations and Native Texts. By Marius Barbeau. Pp. vi + 322 + 14 plates. 3 dollars. (Ottawa: Queen's Printer, 1960.) [2411

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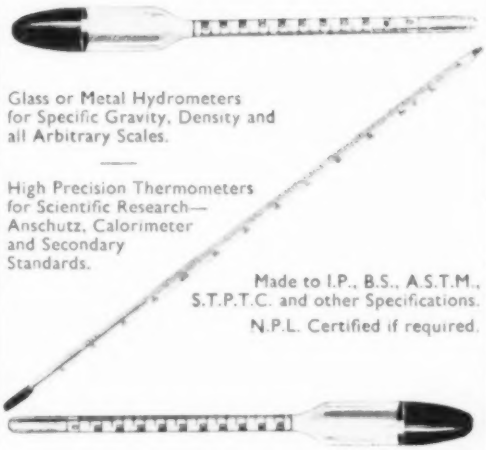

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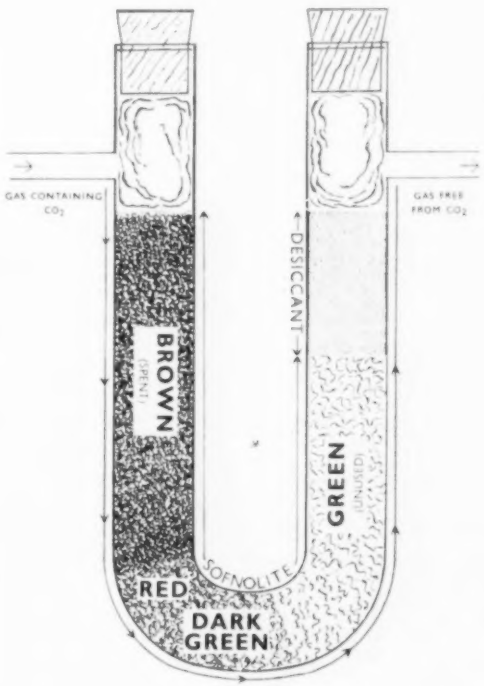

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APPOINTMENTS VACANT

ROYAL NAVAL SCIENTIFIC SERVICE

ADMIRALTY require SENIOR SCIENTIFIC OFFICERS/SCIENTIFIC OFFICERS at

A. UNDERWATER WEAPONS ESTABLISHMENT, PORTLAND, DORSET (Ref. C69/1A)

(1) Mechanical Engineer. Specialized in thermodynamics with experience in internal combustion engine research and/or rocket propulsion field. Minimum five years' experience in either expected. Some experience in appropriate instrumentation essential with design study work on components of rocket systems or other propulsion gear. Turbine design experience advantageous.

(2) Mechanical Engineer with bias for one or more of: (i) hydraulically operated mechanisms, including servo-control; (ii) mechanics of machines (theory and practice); (iii) hydro- (or aero-) dynamics of fairly elementary character.

(3) Hydrodynamicist (or aeronautical engineer), with some years' experience for work on torpedo dynamics.

(4) Mechanical Engineers (servo-mechanisms, gyro design and develop). Electrical Engineers (Electronics/Design). Mathematicians (Operational research and theoretical physics). Physicist (acoustics).

B. GOVERNMENT COMMUNICATIONS H.Q., CHELTENHAM (Ref. A43/1A)

Physicists (Telecommunications). Mathematicians. Electrical Engineers (Electronics/Radar: Telecommunications and Radio).

C. NAVAL CONSTRUCTION RESEARCH ESTABLISHMENT, DUNFERMLINE (Ref. C70/1A)

Structural and Mechanical Engineers, Mathematical Physicists and Mathematicians, for teams engaged on research problems of structural strength, effects of conventional and nuclear weapons and development of new structural materials. Excellent opportunities and good prospects for promotion.

D. ADMIRALTY COMPASS OBSERVATORY, SLOUGH (Ref. D47/1A)

Electrical or Mechanical Engineers or Physicists interested in gyro-techniques, servo-mechanisms or electronics.

Qualifications for all posts first- or second-class honours degree or equivalent in appropriate subject. Must normally be natural born British subjects of natural born British parents. Senior Scientific Officers must have had minimum three years' postgraduate experience and be not less than 26 years of age.

Salaries: (A.) Senior Scientific Officer, £1,302 to £1,604; Scientific Officer, £717 to £1,186. (B, C, D.) Senior Scientific Officer, £1,342 to £1,654; Scientific Officer, £738 to £1,222.

Appointments unestablished (with F.S.S.U. benefits) but opportunities for those between 21 and 32 to compete for established posts.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference and post.

UNIVERSITY OF MANCHESTER

LEVERHULME RESEARCH FELLOWSHIPS IN RADIO-ASTRONOMY

Applications are invited from suitably qualified graduates for two Leverhulme Research Fellowships tenable for a period of three years. The Fellowships will be awarded for research in some aspects of Radio-astronomy, using the Radio-telescope at the University's Nuffield Radio-astronomy Laboratories at Jodrell Bank. The value of the Fellowship will be not less than £1,050 per annum, with membership of the F.S.S.U.

Application forms may be obtained from the Registrar, the University, Manchester 13, to whom all applications should be sent not later than March 7, 1961.

BRITISH PETROLEUM COMPANY LIMITED has a vacancy for a Chemist at the Research Centre, Sunbury-on-Thames. Applicants should have an honours degree in chemistry and not be more than 30 years of age. A postgraduate training is desirable with experience in the manipulation of electron spin resonance equipment and interpretation of the measurements. The job requires an interest in the application of electron spin resonance techniques to a variety of physico-chemical systems including, for example work with a linear accelerator on radiolysis of hydrocarbon and sulphur compounds. Salary according to age, qualifications and experience. Non-contributory pension fund. Housing scheme, luncheon club. Removal expenses and settling-in allowance payable in certain cases.—Write, giving full details, quoting reference H.5377, to Box 6542, c/o Hanway House, Clark's Place, E.C.2.

Bacteriologist

Birds Eye Foods Limited require a Bacteriologist at their Gt. Yarmouth factory. The vacancy has been created due to promotion. The successful candidate will be responsible to the Quality Control Manager for the bacteriological and chemical control of all the factory products; he will also be responsibe for the organization and supervision of Laboratory work.

Applications are invited from graduates in bacteriology or microbiology and previous experience in the food industry is an advantage.

Written applications should be made to the Personnel Manager, Birds Eye Foods Ltd., South Denes, Gt. Yarmouth, quoting reference GDS/24.

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES FACULTY OF MEDICINE TECHNICAL OFFICER IN MICROSCOPIC PATHOLOGY

The University invites applications for appointment to the position of Technical Officer (Microscopic Pathology) in the newly established School of Pathology at Kensington. Salary: £A.1,213 range £A.1,776 per annum. Commencing salary according to qualifications and experience. Applicants should possess a university degree and/or diploma in medical technology; previous experience in histochemistry is desirable, though not essential. Duties will include the establishment of a laboratory of microscopic pathology for the preparation of teaching material and the research work of the School as well as the training and supervision of technical assistants. The successful applicant will be expected to take up duties as soon as possible, and subject to satisfactory medical examination will be eligible to join the State Superannuation Scheme. Fares to Sydney will be paid for successful applicant and family.

Four (4) copies of applications, together with a recent photograph and the names of two referees, should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, the University of New South Wales, Box 1, P.O., Kensington, N.S.W., by airmail to reach there before March 31, 1961.

EGERTON AGRICULTURAL COLLEGE

NJORO, KENYA

Applications are invited for the following appointments:

(a) PRINCIPAL—applicants should possess a degree in agriculture, together with wide experience appropriate to the appointment.

Salary: £2,500 per annum under consideration in an upward direction.

(b) LECTURER IN AGRICULTURAL ECONOMICS.

(c) LECTURER IN AGRICULTURAL ENGINEERING AND SURVEYING.

Applicants for (b) and (c) should possess a recognized appropriate university degree, together with postgraduate work and experience commensurate with the appointment.

Salary in each case on scale: £1,440 by £60 to £1,860 under consideration in an upward direction.

A gratuity of 13½ per cent of salary is payable for all posts on completion of contract.

Free passages for appointee and family on appointment, leave and retirement.

For application forms and further particulars apply to:

The Commissioner,
East African Office,
Grand Buildings,
Trafalgar Square,
London, W.C.2.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(Faculty of Technology in the University of Manchester)

RESEARCH FELLOWSHIPS

Applications are invited for the following Fellowships tenable in the Department of Textile Chemistry: (i) The Fellow will be expected to work in the field concerned with the bonding of fibres with polymers and will have opportunity to develop such aspects as the cross-linking of polymers, the adhesion of fibres and the physical properties of bonded materials. Stipend in the range £800 to £1,000 per annum. (ii) The purpose of the Fellowship is to extend the investigations made within the Department into the fundamental mechanisms of Textile Printing, and the work is likely to include studies in dyediffusion and the interchange of moisture between textile materials and steam. Postgraduate research experience in Physical Chemistry is therefore desirable and some acquaintance with critical microscopy could be an advantage. Stipend in the range £800 to £950 per annum.

Application forms and copies of the regulations may be obtained from the Registrar of the College, Manchester, 1, to whom completed forms should be returned by Saturday, March 25, 1961.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(Faculty of Technology in the University of Manchester)

Applications are invited for a Senior Lectureship in Industrial Design within the Division of Civil Engineering and Building in the College, with corresponding title and status in the University of Manchester. The person appointed will be expected to assume responsibility for the new section dealing with Industrial Design under the general direction of Professor Denis Harper. A new postgraduate course and some teaching for other departments in the Faculty will be involved. Applicants should have had some industrial experience in the field of design and some knowledge of ergonomics would be valuable. Salary in the scale £1,975 by £75 to £2,325 per annum. Superannuation under the F.S.S.U. Family allowances.

Further particulars and form of application may be obtained from the Registrar, the Manchester College of Science and Technology, Manchester, 1, to whom completed forms should be returned by Saturday, March 18, 1961.

THE BRITISH PETROLEUM COMPANY Limited has an immediate vacancy for a Female Patent Abstractor Searcher (age 25 to 35). Science degree with chemistry essential. Knowledge of French and/or German and Technical Abstracting desirable. Five-day week; luncheon club with 1s. lunches; non-contributory pension scheme; excellent sports and social facilities.—Applicants should write, stating age, qualifications and experience, quoting H.F.26, to Box 4344, c/o Hanway House, Clark's Place, E.C.2.

SCIENCE AND ENGINEERING GRADUATES

are being recruited for several new openings in the Development Department of Birds Eye Foods Limited. The engineers' work is concerned mainly with process improvement for existing products and the development of production lines for new products. Science graduates will be involved largely with product development.

The opportunities will attract only those likely to find satisfaction from working in a vigorous atmosphere in a rapidly expanding company.

Application form and further details available from the **Personnel Manager, Birds Eye Foods Limited, South Denes, Gt. Yarmouth.**

RADIOLOGICAL PROTECTION

The AUTHORITY HEALTH AND SAFETY BRANCH advises on the standards necessary to ensure protection from ionising radiations, and on the way in which the standards are to be applied to safety evaluation of reactors and plant.

We urgently need suitably qualified men to carry out this programme, and can offer excellent opportunities to people with experience of radioactivity or of radiation measurement and dosimetry.

HARWELL

In the RADIOLOGICAL PROTECTION DIVISION there are vacancies for the following:

(a) A PHYSICIST to lead a team assessing radiation dosimetry techniques and health physics instrument design and specification.

(b) A SCIENTIST to lead a team advising on the control of radiation and radioactive contamination, including monitoring and protective clothing.

(c) A TRAINING OFFICER to advise on radiological protection syllabuses and the technical content of training films, together with some lecturing.

(d) A SCIENTIST to lead a team assessing the environmental aspects of radioactive waste disposal.

(e) A MATHEMATICIAN or Mathematical Scientist to apply mathematical and computer techniques to radiobiological problems, e.g. metabolism and radiation dosimetry of human tissues.

RISLEY

(f) A SCIENTIST for work on health physics assessments associated with nuclear reactors with particular reference to reactor siting.

Posts (a)—(e) will be in the Principal Scientific Officer grade, and post (f) will be in the Senior Scientific Officer grade. Additional Scientists in the Senior Scientific Officer grade are needed.

Applicants should have a first- or good second-class Honours degree and be 26 years of age or over, and have at least three years post-graduate experience. Salaries will be within the following scales: £1,840 *to* £2,590 *or* £1,440 *to* £1,770.

Contributory Superannuation, Staff Housing Schemes.

Please write for application form, quoting reference H.19/J.14 to:

Administration Manager, U.K.A.E.A., Authority Health and Safety Branch, Harwell, Didcot, Berkshire

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF GENETICS

Applications are invited for the post of Lecturer (£1,050 by £50 to £1,400 by £75 to £1,550; £1,550 by £75 to £1,850) or Assistant Lecturer (£800 by £50 to £950) in the Department of Genetics. The appointment will be made from October 1, 1961, or earlier, if possible, and will carry F.S.S.U. and family allowance benefits. Initial stipend will be related to qualifications and experience.

Applications (three copies), naming three referees, should be sent by March 31, 1961, to the Assistant Registrar (Science), the University, Edgbaston, Birmingham, 15, from whom further particulars may be obtained.

UNIVERSITY OF SHEFFIELD

Applications are invited for the Chair of Physics. The person appointed will succeed Professor W. Sucksmith as Head of the Department in October, 1962, but will take up duties in the University on a date arranged to suit his convenience and that of the University, between October, 1961, and October, 1962. Salary in the range £3,200 to £3,600 a year, with F.S.S.U. provision and family allowance. A grant towards removal expenses will be made.

Further particulars may be obtained from the Registrar to whom applications (20 copies—one only from overseas candidates), should be sent by April 15, 1961.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3

RESEARCH FELLOWSHIP IN BIOPHYSICS

Applications are invited from graduates in the Physical or Biological Sciences for a Research Fellowship in Biophysics sponsored by the Nuffield Foundation and tenable in the Department of Physics. It is expected that the Fellow appointed, if not already holding a higher degree, would read for a Ph.D. in Biophysics of the University of London. Salary in the range £700 to £900 according to experience. Superannuation rights may be preserved in certain instances.

Further particulars may be obtained from the Secretary, Chelsea College of Science and Technology, to whom applications should be forwarded within fourteen days of the appearance of this advertisement.

TECHNICAL OFFICER REQUIRED FOR interesting work in the assay, identification and application of new cyclotron-produced isotopes to medical research. Experience in counting techniques is necessary, and in spectrometry desirable, but training will be given. Qualifications, B.Sc., H.N.C., Grad.Inst.P., or equivalent. Salary, depending on age and experience, rising to £1,260, plus London weighting.—Apply Director, Radiotherapeutic Research Unit, Hammersmith Hospital, W.12.

UNIVERSITY OF LEEDS

DEPARTMENT OF AGRICULTURE

BRITISH OIL AND CAKE MILLS RESEARCH FELLOWSHIP

Applications are invited from graduates in agriculture, agricultural science or pure science, preferably with honours, for appointment as B.O.C.M. Fellow, at a salary up to £750 per annum according to age, qualifications and experience, together with expenses on the university scale. The Fellowship will be tenable for one year in the first instance, renewable.

Applications (three copies), stating date of birth, qualifications and experience, together with the names of two referees, should reach the Professor of Agriculture, the University, Leeds, 2 (from whom further particulars may be obtained), not later than March 20, 1961.

ASSISTANT EXPERIMENTAL OFFICERS required at the National Vegetable Research Station, Wellesbourne, Warwick, for the following Sections: Chemistry: To work on chemical, physical and horticultural aspects of field experiments on soils. Physiology: For growth and development studies of vegetable crops. Weeds: For ecological work on weeds. Qualifications: Degree (science or horticulture) or equivalent. Salary in scale £578 per annum at age 21 to £981. Contributory superannuation scheme.—Applications, with names of two referees, to Secretary by March 18, 1961.

Central Electricity Generating Board

Research and Development Department

Berkeley Nuclear Laboratories

PHYSICS DIVISION

Applications are invited for a number of posts in the Physics Division of the Berkeley Nuclear Laboratories, Gloucestershire. Persons appointed will initially work in the following sections, although subsequent transfer between sections will be permissible, depending on the developing interests and abilities of the staff concerned.

A. SOLID STATE PHYSICS

To study the fundamental processes of radiation damage and other related effects in irradiated solids. X-ray and electron microscopy facilities are available.

B. THEORETICAL PHYSICS

To study various theoretical problems of interest to the Laboratory, including reactor physics and the theory of radiation damage.

C. REACTOR PHYSICS

To study experimental sub-critical reactor problems and experiments connected with the Board's reactor programme. In view of the growing demand for reactor physicists, these posts are of considerable interest to young men with energy and ability, who wish to enter this field.

D. INSTRUMENTATION

For work developing nuclear radiation detectors and other specialised nuclear instruments. Preference will be given to candidates who are capable of devising and developing new techniques of measurement.

E. GRAPHITE

To study the fundamental mechanisms of irradiation damage in graphite and the corresponding changes of physical properties. To assess the extent of irradiation damage of the graphite in the Board's reactors.

● **Salaries up to £1,325 per annum will be fully commensurate with experience, ability and qualifications.**

The Board's salary scales for Scientific Staff rise to £2,395 per annum. Opportunities for promotion are excellent and will depend entirely upon the contributions made by the successful candidates to the work of the Department.

Preference will be given to candidates with a good honours degree. They should be under 26 years of age.

Applications, stating age, qualifications, experience, present position and salary, and indicating section of interest, to the Appointments Officer, 24/30 Holborn, London, E.C.1, by March 20. Envelopes should be marked "Confidential Ref. N/73."

WEST AFRICAN INSTITUTE FOR OIL PALM RESEARCH

NIGERIA

Vacancies exist for agricultural specialists: Soil Chemist: For the study and analysis of soil types with a view to improving soil conditions. Candidates must have an honours degree in chemistry, or in natural science including chemistry, with at least two years postgraduate experience or training as a soil chemist. Plant Physiologist: To review present methods of production and investigate ways of increasing the supply of palm wine. Candidates must have a good honours degree in botany or natural science with two years suitable postgraduate training or experience, preferably in plant physiology. All appointments are on contract/gratuity terms for two tours of service of 15 to 24 months in the first instance. Salaries in scale £1,392 to £2,388 per annum. Gratuity £150 for each completed year of service. Outfit allowance £60. Furnished quarters at moderate rental. Free passages for officer and wife and for children under 18 up to cost of two adult passages. Generous leave.

Apply, stating full name and giving brief particulars of qualifications and experience, to Director of Recruitment, Colonial Office, London, S.W.1. Quote BCD.197/199/016/CI.

UNIVERSITY OF MANCHESTER

Applications are invited for the following posts now vacant in the Department of Chemistry in the Faculty of Science: (a) Lecturer in Chemistry; candidates should have special interest in statistical thermodynamics and be willing to teach this subject to third year and postgraduate students. (b) Assistant Lecturer in Chemistry; candidates should have special interest in some branch of physical chemistry. (c) Senior Research Assistant; candidates should have experience in polymer science, and be willing to assist Professor Gee in the supervision of students carrying out research on the physical chemistry of polymers; the post is a temporary one, financed by a grant from D.S.I.R., but the forthcoming expansion of the department will offer good opportunities of permanent posts. Salary ranges: (a) and (c), £1,050 to £1,850 per annum, initial salary according to qualifications and experience; (b) £800 to £950 per annum. Duties to commence as soon as possible. Membership of F.S.S.U. and Children's Allowance Scheme.

Applications should be sent not later than March 7, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

QUEEN'S UNIVERSITY

KINGSTON, ONTARIO, CANADA

DEPARTMENT OF PHYSICS

Applications are invited from experimental and theoretical physicists for two positions from September 1, 1961, in the Department of Physics. Staff is being increased to 15 full-time members. New appointments normally become permanent after two years. Duties will be primarily teaching undergraduate and graduate students, but fundamental research is expected and encouraged. Present research programme includes experimental and theoretical atomic and nuclear physics, solid state physics, and radio astronomy. New physics building has been approved and will be constructed in the immediate future. Salary and rank will depend upon qualifications which should include a Ph.D. degree. Teaching or research experience will be valued. Positions will be in the ranks of Lecturer or Assistant Professor and within the salary range $6,600 to $8,500 per annum.

Applications and inquiries should be addressed to the head of the department.

UNIVERSITY OF BRITISH COLUMBIA

PHYSICS

Applications are invited for appointments to the teaching and research staff as well as for postgraduate fellowships and scholarships for the Session commencing in September, 1961. There are specific vacancies at the Assistant Professor level in Optical Spectroscopy, Meteorology and Low Energy Theoretical Nuclear Physics. Applications in other fields of physics will also be considered.

Further information and a copy of an illustrated brochure describing the activities and facilities of the Department may be obtained by writing to G. M. Shrum, Head, Department of Physics, University of British Columbia, Vancouver 8, B.C. Professor Shrum expects to be in London from March 16 to 25 and will be pleased to arrange personal interviews. Inquiries should be directed to B.C. House, 1 Lower Regent Street, London, S.W.1.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Lecturer or Assistant Lecturer in Anatomy with a special interest in Experimental Neurology: candidates should be medically qualified (with qualifications registrable in this country), and should possess a good knowledge of neuro-anatomy. Good research facilities are available. Salary scales: Lecturer, £1,500 to £2,275; Assistant Lecturer, £1,000 to £1,400. Membership of F.S.S.U. and Children's Allowance Scheme; initial salary according to qualifications and experience. Duties to commence as soon as possible.

Applications should be sent not later than March 11, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained. Overseas applicants should send letters of application in the first instance, giving full details of qualifications and experience, and should submit the names of at least three persons to whom reference may be made.

SOUTH-WEST ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART

FOREST ROAD, WALTHAMSTOW, E.17

Senior Lecturer in Physics required May 1, 1961, or as soon as possible thereafter. Applicants should have an honours degree and suitable teaching and research experience. Higher degrees and specialization in Modern Atomic Physics are additional recommendations. The person appointed will take a major part in teaching B.Sc. General (New Regulations) and Grad.Inst.P. Courses and will be encouraged to undertake research for which considerable facilities are available. Salary within scale £1,550 to £1,750 per annum, plus £38 or £51 London Allowance.

Apply by letter only (no forms) to the Clerk to the Governors, giving details of qualifications, training and experience, together with three recent testimonials or the names and addresses of three referees.

BRITISH COLUMBIA RESEARCH COUNCIL

BIOLOGICAL ENGINEER

The British Columbia Research Council invites applications for an appointment as a Biological Engineer. There are also vacancies in Applied Biology and Bacteriology. Background training in Chemistry or Chemical Engineering with some experience in biochemistry and bacteriology would be desirable for the position in Biological Engineering. The work will include the study of water quality, the design of systems for the treatment of industrial wastes, and the preparation of technical reports. The British Columbia Research Council is a non-profit applied research organization established at the University of British Columbia. The salary range for these positions is $6,500 to $8,500 with the same pension and other benefits in effect at the University. Those interested should write for an illustrated brochure describing the activities and research facilities of the Council.

Applicants should submit full information regarding training and experience to Dr. P. C. Trussell, Head, Applied Biology Division, B.C. Research Council, Vancouver 8, Canada.

UNIVERSITY OF CAMBRIDGE

SCHOOL OF AGRICULTURE

Applications are invited for the post of University Demonstrator in Agricultural Entomology from October 1, 1961. Qualifications should include an honours degree in an appropriate science. Stipend: £980 by £50 to £1,150. Tenure of the post is for a period of five years. An allowance of £50 a year is payable for each dependent child under sixteen or in receipt of full-time education. A limited contribution may be made towards the removal expenses of the successful applicant.

Applications, in writing, with the names and addresses of not more than three referees, should be sent to the Secretary, School of Agriculture, Downing Street, Cambridge, to reach him not later than March 31, 1961.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Technician or Junior Technical Officer (female) required to assist in biological research at Pollards Wood Research Station, Chalfont St. Giles, Bucks. Previous experience in genetics, cytology or histology desirable. Special academic or technical qualifications not essential but "A" level G.C.E., B.Sc., or equivalent an advantage. Permanent and superannuable; salary within M.R.C. scales according to qualifications, age and experience.—Applications to the Secretary, 13 Sumner Place, London, S.W.7, by March 10, quoting ref. 301/B/52.

ANIMAL NUTRITIONIST

SILCOCKS, OF LIVERPOOL, invite applications for a vacancy on their Research Staff for a first-class Animal Nutritionist. Applicants should be in the thirties, and must have a good academic and practical training in Animal Nutrition and experience in the formulation of rations for farm livestock.

DUTIES

The successful applicant will be directly responsible to the Technical Director, and will be required to:

- Keep himself fully informed, through the study of current literature and by personal contact with Research Centres, of the latest information on Animal Nutrition.
- Assist in the preparation of diets for different classes of stock, using the most recent knowledge of nutritional requirements.
- Work with our Experimental Farms and Laboratories on the planning of feeding trials and the interpretation of results.

SALARY

The starting salary will be a generous one in keeping with the applicant's qualifications and experience and the importance of the work involved. The conditions of working and general facilities are excellent, and the post carries the benefits of the Company's excellent Pension Scheme.

PROMOTION

This is a post of increasing responsibility and offers opportunities of considerable promotion to the right man.

APPLICATIONS

Applications, which will be treated in strict confidence, should be addressed to:

Technical Director, R. Silcock & Sons Ltd., Stanley Hall, Edmund Street, Liverpool, 3.

THE MOND NICKEL COMPANY LIMITED

requires a young male or female

ABSTRACTOR/TECHNICAL WRITER

to assist in the preparation of publications covering metallurgical literature relevant to the Company's activities. Ability to write concise, clear English is essential for the post, and a knowledge of German and French desirable.

Applications, giving full details, should be addressed to the General Manager, Development and Research Department, The Mond Nickel Company Limited, Thames House, Millbank, London, S.W.1. Mark envelope "Confidential M.10."

PROGRESSIVE PHARMACEUTICAL COMPANY

in South Cheshire requires a Chemist (Hon.B.Sc. or A.R.I.C.) to work on own initiative under supervision of a research manager. The duties would require the applicant to interest himself in a wide range of problems connected with the development and control of pharmaceuticals including biological materials.

Experience of modern analytical techniques would be an advantage. The post is permanent, pensionable and offers real interest and excellent prospects to the right man who should be 25 to 30 years of age.

Applications, which should be submitted in full, will be treated in the strictest confidence. Write to Box No. 952, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

PHYSICAL CHEMIST

The Organization's **Division of Coal Research, North Ryde, Sydney, N.S.W.**, invites applications for the position of Physical Chemist from Honours graduates in Science, majoring in Physical Chemistry (or equivalent qualifications) with postgraduate research experience. Experience in gas-phase and gas-solid kinetics and infra-red spectroscopy an advantage.

The appointee will be required to initiate and carry out research concerned with the chemical constitution and the mechanism of pyrolysis, oxidation and hydrogenation of coal. Particular emphasis will be placed on novel physico-chemical methods for which a wide range of equipment is available including apparatus for U.V., infra-red, emission and mass spectroscopy.

SALARY: dependent on qualifications and experience within the ranges: £A.1,510 to £A.2,265 or £A.2,395 to £A.2,720 per annum.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further particulars of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No.: 480/3580) should be addressed by April 15, 1961.

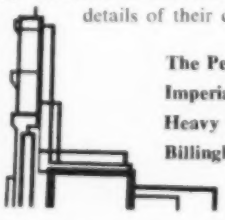
HEAVY ORGANIC CHEMICALS DIVISION

This Division is already a major producer of petroleum chemicals, providing raw materials for plastics, paints, synthetic rubbers and synthetic fibres. It has a large Research Department with an extensive programme of work on new and existing products. To expand this work it is seeking

RESEARCH CHEMISTS

The problems to be tackled cover a wide range where a broad knowledge of organic, inorganic and physical chemistry can be fully utilized. There is scope for original work on polymerisation, oxidation, carbonylation, pyrolysis and catalysis as well as for the discovery of new reactions and for study of the underlying chemistry of existing ones.

Men and women who have good honours degrees, and who would be interested in this kind of work, are invited to write, giving brief details of their qualifications and experience, to



The Personnel Manager,
Imperial Chemical Industries Limited,
Heavy Organic Chemicals Division,
Billingham, Co. Durham.

quoting reference MB/RC/7.

UNIVERSITY COLLEGE OF GHANA

FACULTY OF AGRICULTURE

Applications are invited for:

(i) Lectureship or Assistant Lectureship with responsibility for teaching Animal Nutrition. Applicants should possess honours degree in chemistry or biochemistry or alternatively honours degree in agriculture followed by specialization in animal and human nutrition.

(ii) Senior Lectureship in Crop Production. Candidates should preferably possess a higher degree or an honours degree in agriculture or alternatively a higher degree in pure science subject and, in addition, considerable postgraduate experience in some aspect of Tropical Crop Production.

(iii) Lectureship in Plant Pathology. The successful applicant, who preferably should have served in the tropics, should possess an honours degree in pure science with experience in the field of agriculture or alternatively an honours degree in agriculture with specialization in plant pathology.

Salary scales (under review) Senior Lecturer, £G.1,700 by £G.75 to £G.2,150 per annum. Lecturer, £G.1,000 by £G.50 to £G.1,350 (bar) by £G.75 to £G.1,800; £G.1,850 per annum. Assistant Lecturer, £G.900; £G.950 per annum, entry point according to qualifications and experience. F.S.S.U. Outfit, family and other allowances. Passages for appointee and family on appointment, leave and normal termination. Part-furnished accommodation at a charge not exceeding 7.5 per cent of salary.

Detailed applications (six copies), naming three referees, by March 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Experimental Officer in the Department of Chemistry in the Faculty of Science. Candidates should preferably have experience of quantitative work on the physical properties of polymers; minimum academic qualification is the Higher National Certificate; the person appointed would be required to assist in research work in polymer science, especially in connection with polymer characterization. The post is at present temporary, but it is hoped that a permanent appointment will be available later. Salary range: £700 to £1,000 per annum; initial salary according to qualifications and experience, and a lower starting salary could be offered if the selected candidate had no previous experience. Duties to commence as soon as possible.

Applications should be sent not later than March 7, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

OLDCHURCH HOSPITAL ROMFORD, ESSEX

(709 Beds)

RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

UNIVERSITY COLLEGE OF SIERRA LEONE

FOURAH BAY COLLEGE

Applications are invited for a Lectureship in each of the following: Botany: interest in ecology or cryptogamic botany or applied botanical field (agriculture, forestry or horticulture) with interest in physiology of growth. Geography: an appointment on secondment for one session or more considered. Zoology. Salary scale: £965 by £50 to £1,415; £1,495 by £75 to £1,790 per annum, entry point according to qualifications and experience. Negotiations in progress for salary revision. F.S.S.U. Outfit and family allowances (maximum £300). Passages on appointment, annual leave and normal termination. Part-furnished accommodation at reasonable rent.

Detailed applications (six copies), naming three referees, by March 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

FELLOWSHIPS FOR RESEARCH IN ELECTROCHEMISTRY

A number of Fellowships for Graduate Students are being offered by the Electrochemistry Research Group of the Chemistry Department at the University of Pennsylvania. They are open to competition from students who can produce evidence of exceptional ability such as a first-class honours degree in physics, chemistry or metallurgy. Research work will be selected from the following fields: electrode kinetics, semiconductor-electrolyte interface, structure of molten electrolytes, and adsorption at the metal-electrolyte interface. Travel costs to and from Philadelphia will be paid for successful applicants. The research work will be suitable to form the basis of a Ph.D. thesis. During the first year, candidates must pass qualifying examinations of high standard in theoretical chemistry before they are further considered for the research degree. All University fees will be paid, and the yearly stipend will be $3,600.

Applicants should write to Mr. James Malone, Department of Chemistry, John Harrison Laboratory of Chemistry, University of Pennsylvania, Philadelphia 4, Pa., before April 1, 1961.

FEDERAL GOVERNMENT OF NIGERIA

DEPUTY DIRECTOR OF AGRICULTURAL RESEARCH

Required for the Department of Agricultural Research, Moor Plantation, Ibadan, to assist the Director of Agricultural Research in administrative duties. Candidates should have an honours degree in natural science, together with considerable postgraduate research experience, preferably not less than ten years. Candidates must have shown an aptitude for directing research investigation and preference will be given to those possessing a flair for administration. The possession of a postgraduate research degree would be an advantage.

Appointment on contract for one tour of 12 to 18 months in the first instance with prospect of extension. Salary £2,748 per annum. Free passages for officer and wife. Children's allowances whilst separated. Liberal home leave on full pay. Income tax at low local rate. Quarters at low rent.

Write for application forms and further particulars within ten days of publication, stating briefly age, qualifications and experience, to the Recruitment Attaché, Office of the High Commissioner for Nigeria, Nigeria House, 9 Northumberland Avenue, London, W.C.2, quoting B.14/1.

ST. ALBANS CITY MUSEUM

APPOINTMENT OF ASSISTANT CURATOR IN NATURAL HISTORY

Applications are invited for the post of Assistant Curator in Natural History. Applicants should have a university degree in biology and the Diploma of the Museums Association. The post offers considerable opportunities, involves the reorganization of the Department and the inauguration of the Schools Service. The salary will be within APT II (£815 to £960) the commencing rate being determined by ability and experience, and the appointment will be subject to the National Scheme of Conditions of Service and Local Government Superannuation Acts. Further particulars can be supplied by the Director of Museums, Verulamium Museum, St. Albans.

Applications, giving fullest details of education and experience, together with the names of three references, should reach the undersigned by March 31, 1961.

B. V. ENTWISTLE,
Town Clerk.

38 St. Peter's Street,
St. Albans.

UNIVERSITY OF LEEDS

DEPARTMENT OF INORGANIC AND STRUCTURAL CHEMISTRY

Senior Research Assistant wanted as soon as possible to join a team doing research in high pressure chemistry, with some applications to geochemistry. Appointment for one year, with possibility of extension. A preference will be given to applicants who have done research in the field of high pressure geochemistry.

Applications should be sent direct to Dr. R. S. Bradley, Department of Inorganic and Structural Chemistry, the University, Leeds, 2, England.

THE PATENT OFFICE

offers an interesting, well paid job with good prospects to suitably qualified men and women in congenial working conditions.

interest

You will be dealing with inventions from the whole world in your chosen subject. By its very nature the work will inevitably maintain your knowledge of science and technology completely up to date and will give you inside knowledge of new manufactures well ahead of the public at large.

salary

The training salary for the first two years is £793 and £824. On satisfactory completion the scale is £941–£1,719 by regular increments, but there is a jump in the scale to £1,324 five years after entry, or only four or even three in cases of special merit. Approved postgraduate experience fetches a higher starting salary. One promotion only, of which prospects are excellent, raises your maximum to £2,715. Reasonable proportion of still higher posts up to £3,865 all filled exclusively by promotions from entry grade.

qualifications

Age 21–36 and first- or second-class honours degree in physics, chemistry, engineering or mathematics, or an equivalent such as A.R.I.C., A.Inst.P., or corporate membership of I.C.E., I.Mech.E., or I.E.E., or first- or second-class honours Diploma of Technology.

conditions

Location, London, five-day week. Annual leave 4½ rising to 6 weeks. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information, or for a visit to the Patent Office to see the work, entirely without obligation. **The Superintending Examiner (B Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Telephone** HOLBORN 8721. **Ext.** 324.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Assistant Experimental Officer required in Chemical Microbiology Department for work on cheese flavour. Candidates should be familiar with elementary chemical techniques and should possess pass degree or equivalent, or if under 22 G.C.E. "A" level in two subjects. Starting salary within range £450 10s. (at 18) to £776 (at 26), in scale to £983; pension scheme; five-day week.

Apply to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/9.

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF GEOLOGY

Applications are invited for the post of Research Fellow in the Department of Geology. Candidates will be considered without restriction as to their particular field of interest in geology. The stipend, within the range of £800 to £900 per annum, will be related to qualifications and experience, and the appointment will carry F.S.S.U. and family allowance benefits. The appointment will date from October 1, 1961.

Applications (three copies), with the names of three referees, should be sent before March 31, 1961, to the Registrar, the University, Edgbaston, Birmingham 15, from whom further particulars may be obtained.

UNIVERSITY OF ALBERTA

DEPARTMENT OF CHEMISTRY TEACHING ASSISTANTSHIPS

$2,200 to $2,700 for eight months are open to qualified students proceeding to advanced degrees. Nine hours per week of laboratory instruction required. Active research programmes in analytical, inorganic, organic, physical and theoretical chemistry. Travel allowance.

Apply to: Professor Harry E. Gunning, Head, Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada.

THE SCIENTIFIC CIVIL SERVICE NEEDS men and women for pensionable posts as (a) Experimental Officers and (b) Assistant Experimental Officers in mathematics, physics, meteorology, chemistry, metallurgy, biological sciences, engineering, miscellaneous (geology, library and technical information services). Candidates must, on December 31, 1961, be at least 26 and normally under 31 for (a), and at least 18 and normally under 28 for (b). Qualifications should normally include H.S.C., or G.C.E., or equivalent, or H.N.C., a University degree, or a Diploma in Technology. Provisional admission if taking examinations in 1961. London salary scale (a) £1,117 to £1,376; (b) £465 10s. (at 18) to £826 (26 or over) rising to £1,009. Promotion prospects. Further education facilities.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form, quoting **S/94-95/61**.

ESSEX

MID-ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART
MARKET ROAD, CHELMSFORD

Applications are invited for the following new posts from September 1, 1961:

SCIENCE DEPARTMENT

1. Senior Lecturer in Chemistry to teach up to H.N.C. and B.Sc. (General) degree level and to be responsible for the organization of the Chemistry Section of the Department. Applicants should be well-qualified academically and should have had appropriate teaching and research or industrial experience.

2. Lecturer in Physics to teach up to H.N.C., B.Sc. (General) degree and Sandwich Diploma level. Applicants should have a good honours degree, with research or industrial experience, and be able to teach a branch of Applied Physics, preferably High Vacuum Technology.

Salaries in accordance with the 1959 Burnham Report: Senior Lecturers, £1,550 by £50 (4) to £1,750. Lecturers, £1,370 by £35 (4) and one final increment of £40 to a maximum of £1,550.

Particulars and forms of application (to be returned in fourteen days), from the Clerk to the Governors at the College.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for Imperial Chemical Industries Fellowships tenable at the University College of North Staffordshire. Fellowships may be awarded for the purpose of carrying out original research in chemistry or physics, for a period not exceeding three years. Applicants should preferably hold the degree of Ph.D. or have equivalent research experience. Annual stipend will depend upon age, qualifications and experience, but will be within the range £800 to £1,100, together with F.S.S.U. benefits.

Applications (two copies), stating age, details of education, career and qualifications, publications and an outline of the proposed research, together with the names of two referees, should reach the Registrar, University College of North Staffordshire, Keele, Staffs, from whom further inquiries may be made, not later than March 31, 1961.

UNIVERSITY OF HULL

DEPARTMENT OF MATHEMATICS
LECTURESHIP IN APPLIED MATHEMATICS
LECTURESHIP OR ASSISTANT LECTURESHIP IN PURE MATHEMATICS
LECTURESHIP OR ASSISTANT LECTURESHIP IN PURE OR APPLIED MATHEMATICS

Applications are invited for the above posts, tenable from October 1, 1961. Salary: Lecturer, £1,050 to £1,850 per annum; Assistant Lecturer, £800 to £950 per annum, with placing according to qualifications and experience; F.S.S.U. and family allowances.

Further particulars may be obtained from the undersigned to whom applications (eight copies) should be submitted by March 29, 1961.

W. D. CRAIG,
Registrar.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

Assistant Experimental Officer required in physics department to assist in studies of physical properties of dairy products—butter and cheese, etc. He will also be required to construct and modify experimental testing equipment in the department workshop, and skill in using a lathe would be advantageous. Candidates should possess H.N.C. or pass degree, or if under 22 G.C.E. "A" level or equivalent. Starting salary within range £450 10s. (at 18) to £776 (at 26) in scale to £983; pension scheme.

Apply, naming two referees to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/4.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in animal physiology, embryology and histology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September, 1961, to include teaching and research. The starting salary will be based on qualifications and experience.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

THE REED PAPER GROUP

has a vacancy for a

TECHNICAL EDITOR

Reed

in one of the Research and Development Departments in the organization.

The work will cover the editing of reports written by technical personnel and will also involve, as necessary, the actual writing of technical reports given the requisite background data and material. The work will develop into a kind, eventually, of exceptional interest. A very high standard will be required.

Experience is essential and candidates (these may be of either sex) should hold a science degree or have a relevant technical background. Previous experience in abstraction and information work would be an advantage. The appointment will be tenable at Aylesford, near Maidstone in Kent.

Excellent conditions of service include assistance with house purchase and non-contributory Pension Fund.

Applications, stating academic qualifications and career to date, should be addressed to:

The Group Personnel Officer,

Albert E. Reed & Co. Ltd.

Larkfield, Nr. Maidstone, Kent

quoting reference TE/PDDD/63

MULLARD RESEARCH LABORATORIES

Mullard

SOLID STATE PHYSICS DIVISION

have vacancies for

INORGANIC and PHYSICAL CHEMISTS

to join teams doing basic research in the solid state. Topics include semiconducting compounds, crystal growth by vapour deposition, and magnetic and other oxides, including the preparation of single crystals.

The work is extremely varied and its chemical aspects are becoming ever more important.

Applicants should have a first- or second-class honours degree. There are openings for recent graduates and for experienced research chemists.

Applications, quoting ref. KH/2, to:

Mr. G. A. Taylor,
Mullard Research Laboratories,
Cross Oak Lane, Salfords, nr. Redhill, Surrey.

UNIVERSITY OF DURHAM

KING'S COLLEGE
NEWCASTLE UPON TYNE

Applications are invited for a Fellowship or Research Associateship in the Department of Chemistry. The applicant should possess a Ph.D. or equivalent qualification in biochemistry or organic chemistry. The work will be concerned with various aspects of the structure and function of nucleotides in micro-organisms, sugar biosynthesis or bacterial cell walls. The salary will be within the range of £800 to £1,000 per annum, with membership of F.S.S.U. if required.

Applications, which should include the name of at least one referee, should be sent to the Professor of Organic Chemistry, King's College, Newcastle upon Tyne, 1.

UNIVERSITY COLLEGE LONDON, GOWER Street, W.C.1. Applications are invited for the following posts in the Department of Botany, duties to commence October 1, 1961. (1) Lecturer in Microbiology, salary £1,050 to £1,850 plus £60 London allowance. Interest in structure or genetics of bacteria or viruses. (2) Assistant Lecturer in Plant Ecology. Salary £800 to £950 plus £60 London allowance. F.S.S.U. and family allowance for both posts.—Applications should be sent by April 15 to the Secretary, from whom further particulars may be obtained.

UNIVERSITY OF BIRMINGHAM

TEMPORARY LECTURESHIPS IN PURE MATHEMATICS

Applications are invited for three posts of Temporary Lecturer (stipend within the range £1,050 to £1,550) or Temporary Assistant Lecturer (£800 to £950) in the Department of Pure Mathematics. Stipends will be related to qualifications and experience and the appointments will be for a period of one or two years and may carry F.S.S.U. and family allowance benefits.

Applications (three copies), with names of three referees, should be sent by March 31, 1961, to the Assistant Registrar (Science), the University, Edgbaston, Birmingham, 15, from whom further particulars may be obtained.

APPLICATIONS ARE INVITED FOR A post of Research Assistant in connection with a grant awarded by the Nature Conservancy to the British Phycological Society to enable work to be carried out on the preparation of a new Flora of British Marine Algae, principally the Rhodophyta volume of this Flora. The maximum salary will be £700 per annum, together with F.S.S.U. The post will be tenable year by year for three years.—Applications, stating age, academic qualifications and experience, together with the names of two referees, should be received by the Registrar, the University, Liverpool, 3.

UNIVERSITY COLLEGE OF GHANA

Applications are invited for (a) Lectureship or (b) Assistant Lectureship in Zoology. Preference given to candidates with special interests in cytology and genetics or invertebrate zoology. Salary scales (under review): (a) £G.1,000 by £G.50 to £G.1,350 by £G.75 to £G.1,800; £G.1,850 per annum. (b) £G.900; £G.950 per annum. Entry point according to qualifications and experience. F.S.S.U. Outfit, family and other allowances. Passages for appointee and family on appointment, leave and normal termination. Part-furnished accommodation at a charge not exceeding 7.5 per cent of salary.

Detailed applications (six copies), naming three referees, by March 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

BIRKBECK COLLEGE
(UNIVERSITY OF LONDON)

Applications are invited for the following posts: Assistant Lecturer or Lecturer in Statistics. Assistant Lecturer in Psychology. Assistant Lecturer in Zoology. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,550 (efficiency bar) £1,625 by £75 to £1,850 per annum. Assistant Lecturer, £800 by £50 to £950 per annum. London allowance of £60 per annum is payable in addition in both grades.

Candidates should obtain particulars from the Secretary, Birkbeck College, Malet Street, W.C.1. Closing date for all applications March 18, 1961.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for the post of Lecturer or Assistant Lecturer in Mathematics. Applicants should be qualified in Pure or Applied Mathematics. The appointment will start from October 1, 1961. Salary in scale £1,050 by £50 to £1,400 by £75 to £1,850 (Lecturers), £800 by £50 to £950 per annum (Assistant Lecturers), with F.S.S.U. and children's allowances.

Applications should reach the Registrar, the College, Keele, Staffs, from whom further particulars and application forms may be obtained, not later than March 25, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for the post of Research Assistant in the Gatty Marine Laboratory, St. Andrews. Candidates should be suitably qualified in mathematics, physics or zoology for work on the analysis of the nervous system of lower animals. The successful candidate may register for a higher degree. Salary scale up to £750 per annum according to qualifications; appointment for three years in the first instance.

Applications, with names of three referees, should be lodged not later than March 13, 1961, with the Joint Clerk to the University Court, College Gate, St. Andrews.

INSTITUTE OF CHILD HEALTH
(UNIVERSITY OF LONDON)

Applications are invited for the post of Senior Technician (Whitley Scales) to assist in work on lung function. Applicants should have had experience in a physiological laboratory.

Apply to the Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond Street, W.C.1.

RESEARCH ASSISTANT WANTED AT Stoke Mandeville Hospital to help with current research on an immunological project connected with Rheumatoid Arthritis. The person appointed would work directly with the Pathologist undertaking the research. Salary £750 to £1,000 per annum according to qualifications.—Inquiries and applications, giving details of experience and the names of two referees, to the Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

NATIONAL CHEMICAL LABORATORY (D.S.I.R.), Teddington, Middlesex, requires Assistant Experimental Officer to join team studying influence of micro-organisms on corrosion of metals, particularly in soil. Should be microbiologist with experience in isolation and maintenance of pure bacterial cultures. Experience in biochemical techniques advantageous. Work involves fundamental investigations in laboratory and practical application in the field. Qualifications: Over age 22, pass degree or H.N.C. in appropriate subject expected, with interest in biological subjects. Salary range: £680 (age 22) to £841 (age 26) to £1,023.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1. Quoting G.46/1A. Closing date March 18, 1961.

SOUTH-WEST ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART
FOREST ROAD, WALTHAMSTOW, E.17

Senior Lecturer in Applied Biochemistry required as soon as possible. The person appointed will be responsible for the teaching of Biochemistry and related subjects, Paper Chromatography, Low and High Voltage Paper Electrophoresis, and Vapour Phase Chromatography, to H.N.C., B.Sc., and Grad.R.I.C. students and in the Laboratory Technician courses as well as in the Special and Post-graduate courses. Experience in the field of nucleic acid chemistry, enzyme chemistry, or radioactive tracer techniques, or interest in electronic instrumentation, is an added recommendation. Candidates should possess high academic qualifications, have teaching experience and provide evidence of research ability. Considerable research facilities are available and fundamental research will be encouraged. Salary within scale £1,550 to £1,750 per annum, plus £38 or £51 London allowance.

Apply by letter only (no forms) to the Clerk to the Governors, giving details of qualifications, training and experience, together with three recent testimonials or the names and addresses of three referees.

MACAULAY INSTITUTE FOR SOIL RESEARCH

Applications are invited from male graduates possessing a first- or second-class honours degree with physical or inorganic chemistry as the principal subject, for the post of Scientific Officer in the Department of Pedology. The work will involve investigations upon soil formational processes with a physico-chemical bias. The salary will be within the range £710 to £1,175 according to age, qualifications and experience. Superannuation under F.S.S.U.

Forms of application may be obtained from the Secretary, the Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen, to whom they should be returned before March 31, 1961.

MEMORIAL UNIVERSITY OF NEWFOUNDLAND
ST. JOHN'S, NEWFOUNDLAND, CANADA

Applications are invited for the position Assistant Professor of Biology with specialization in invertebrate zoology. Candidates with background and experience in marine biology will receive preference. Ph.D. or equivalent essential. Duties beginning September, 1961, to include teaching and research.

Applications, accompanied by complete curriculum vitae and the names of three references, should be addressed to the Head, Department of Biology, Memorial University of Newfoundland.

LOUGHBOROUGH COLLEGE OF TECHNOLOGY
LEICESTERSHIRE
PHYSICAL EDUCATION AND INDUSTRIAL FITNESS DEPARTMENT
RESEARCH APPOINTMENTS FROM SEPTEMBER, 1961

Suitably qualified persons are invited to undertake work in any of the following fields:
Applied Physiology
Anthropometry
Industrial Recreation
Physical Education

Two appointments are available, for two years initially, and then subject to review, either as Research Scholar, value £350 to £500 per annum, plus possibility of payment for some teaching duties,
or as Research Assistant, £520 to £1,000 per annum, with superannuation.

Further particulars from Academic Registrar, quote Ref. 3/AF.

UNIVERSITY OF BRISTOL
DEPARTMENT OF PHYSICAL AND INORGANIC CHEMISTRY
BRITISH TITAN PRODUCTS POST-DOCTORAL RESEARCH FELLOWSHIP

Applications are invited for a post-doctoral Fellowship for research on photo-adsorption and photo-catalysis at titanium oxide surfaces. The appointment will date from October, 1961, and will be for a period of one year in the first instance with the possibility of extension for a second year. The successful applicant will work in collaboration with Dr. F. S. Stone and the value of the Fellowship will be in the range £700 to £800, according to age and experience.

Applications, giving full academic qualifications, details of research experience, and the names of two referees, should be sent to the Registrar, the University, Bristol 8, England.

SOUTH-EAST ESSEX TECHNICAL COLLEGE
LONGBRIDGE ROAD, DAGENHAM

Required in September: A Senior Lecturer in Chemistry, to specialize in Inorganic or Physical Chemistry. Good honours degree, or equivalent, essential, with appropriate teaching experience. Ability to teach to Grad.R.I.C. and B.Sc. General standard essential. Industrial experience and/or postgraduate research experience desirable. Salary £1,550 by £50 to £1,750 per annum plus London allowance (£38 or £51 per annum).

Application forms and further particulars from the Clerk to the Governors at the College.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

Scientific Officer with good honours degree in biochemistry or chemistry and with particular interest in lipid metabolism required to investigate the interrelationship between sterol and fatty acid metabolism in animals. Appointment for three years at salary commensurate with age and experience within the scale £717 per annum to £1,222. Facilities exist for registration for higher degree.

Apply, naming two referees, to Secretary, National Institute for Research in Dairying, Shinfield, Reading. Quote reference 61/7.

UNIVERSITY OF ABERDEEN
DEPARTMENT OF CHEMISTRY

Applications are invited for the post of Lecturer in Chemistry (Inorganic). Salary £1,050 to £1,850 with placing according to qualifications and experience. F.S.S.U., children's allowance and removal allowance.

Particulars from the Secretary, the University, Aberdeen, with whom applications (eight copies), should be lodged not later than March 25, 1961. Applicants outside the British Isles may submit one copy.

UNIVERSITY OF LONDON
INSTITUTE OF DISEASES OF THE CHEST

Laboratory Technician with general experience required for Clinical Immunology Laboratory, to assist in research into components of fungi in relation to human disease. Salary on Whitley Council scale.

Apply: Secretary, Institute of Diseases of the Chest, London, S.W.3.

AEON LABORATORIES HAVE A NUMBER of vacancies as a result of further expansion.

(a) Physicists for research projects in the field of metal physics. One vacancy is for a graduate skilled in electron microscope applications to problems.

(b) Metallurgists interested in electron metallographic studies of ferrous materials, or in advanced projects on sintered metal compacts.

(c) Research Assistants for the operation of instruments requiring delicate manipulation and for application of standard techniques and development of new ones in several interesting research projects. A sound grasp of elementary physics is required, and an interest in crystallography, structure of metals, and vacuum techniques would be a great advantage.

(d) Technologists skilled in the preparation of samples for electron microscopy, and particularly with skill in microtomy are required.

Applicants for vacancies (a) and (b) should have a good honours degree or equivalent qualifications (A.Inst.P., or A.I.M.).

For vacancies (c) and (d) applicants should possess O.N.C. or H.N.C. in Applied Physics or Metallurgy, or "A" level G.C.E. in Physics, Chemistry and Mathematics.

All the posts are open to men or women. The prospects in this expanding organization are excellent for those with real ability; the salaries are high, and working conditions pleasant. Pension scheme. Five-day week.—Apply Aeon Laboratories, Beech Hill, Ridgemead, Englefield Green, Egham, Surrey.

CHEMICAL RESEARCH ASSISTANT/TECHnician, preferably with experience of steroid chemistry, to work with team investigating aspects of chemical endocrinology in relation to human biology and genetics.—Apply, giving two referees, Dr. J. M. Tanner, Institute of Child Health, Great Ormond Street, W.C.1. Closing date March 10.

BEDFORD COLLEGE (UNIVERSITY OF London), Regent's Park, N.W.1. Applications are invited for the post of Laboratory Technician in the Department of Chemistry. Relevant experience desirable. Salary according to qualifications and experience.—Apply the Secretary.

UNIVERSITY OF LONDON

INSTITUTE OF DISEASES OF THE CHEST

Applications are invited from a Biologist or Mycologist with chemical experience or Chemist to assist in Clinical Immunology Laboratory in research into components of fungi in relation to human disease. Post suitable for graduate wishing to proceed to Ph.D. Immunological experience not essential. Salary on University scale.

Applications addressed to: Secretary, Institute of Diseases of the Chest, Brompton, London, S.W.3.

UNITED KINGDOM TECHNICAL ASSISTANCE

ADVISER ON SCIENTIFIC PUBLICITY required by the MINISTRY OF ECONOMIC DEVELOPMENT OF THE GOVERNMENT OF THE FEDERATION OF NIGERIA

Applicants should either be Journalists with some Scientific qualifications or Scientists with a flair for Journalism. Salary £2,500 per annum plus tax free allowances of £1,730 (married) or £1,045 (single), and allowances for dependent children. Free furnished accommodation is supplied or 45 per cent of basic hotel bills refunded. All emoluments paid by the British Government. Duration: two tours of fifteen months.

For further information and application form, write to Ministry of Labour (E9), 26-28 King Street, London, S.W.1, quoting E9/NTA/NIG/889.

MOREDUN INSTITUTE

EDINBURGH

Physiologist for research appointment. Wide choice of interest including neurophysiology of sheep. Good degree in physiology or M.R.C.V.S. with postgraduate research experience. Salary according to age and qualifications within Senior Scientific Officer/Principal Scientific Officer range: £1,342 to £2,418. F.S.S.U.

Apply in writing to the Secretary, Animal Diseases Research Association, Moredun Institute, Gilmerton, Edinburgh, 9.

LABORATORY SUPERVISOR

(PHYSICIST)

required for Boys' Boarding School. Applicants must have previous experience and be able to supervise technical staff and assume responsibility for maintenance of stock and apparatus for the whole Science School. The Laboratories are new and extensive, and the appointment provides a first-class opportunity.

Apply in writing to the Bursar, Bryanston School, Blandford, Dorset, from whom further particulars of the appointment may be obtained.

MEDICAL RESEARCH COUNCIL require a Scientist for work on radiation induced mutations in microbial populations. Research experience in microbiology or biochemistry essential. Starting salary in range £800 to £1,250 according to age and experience.—Applications, giving full details of qualifications and experience, and the names of two referees to: Administrator, Radiobiological Research Unit, Medical Research Council, Harwell, Berks, as soon as possible.

STOKE MANDEVILLE HOSPITAL

AYLESBURY

Assistant Biochemist required in the Area Pathology Laboratory based at the above Hospital. Applicants should possess first- or second-class honours degree in chemistry or biochemistry, or A.R.I.C. Whitley Council conditions of service. Salary £925 to £1,150 per annum after (for new entrants only) a probationary period. The post offers a wide variety of experience in a well-equipped and pleasant laboratory.

Applications, giving full details of qualifications, etc., together with names of two referees, to be forwarded to the Administrative Officer as soon as possible.

BRITISH PAPER AND BOARD INDUSTRY

RESEARCH ASSOCIATION

MATHEMATICIAN with honours degree and preferably research experience required to join a fundamental research team working on the geometrical and mechanical properties of random fibrous networks.

Apply to the Director (Ref. DHP), B.P.&B.I.R.A., Welcomes Road, Kenley, Surrey.

BEDFORD COLLEGE

(UNIVERSITY OF LONDON)

REGENT'S PARK, N.W.1

The Council invites applications from Honours Graduates for a Lectureship in Physics, vacant October 1, 1961. Open to men and women. Salary scale, £1,050 to £1,850; plus £60 per annum London allowance. Initial salary according to qualifications and experience. Closing date for applications April 15, 1961.

Full particulars from the Secretary.

RESEARCH ASSISTANT WITH B.SC. DEGREE in chemistry or a General B.Sc. degree with chemistry as one subject, required for Medical Professorial Unit to undertake work in the field of human intermediary metabolism. Salary on the scale £665 to £800 per annum.—Applications, in writing, to the Secretary, the Medical College of St. Bartholomew's Hospital, West Smithfield, E.C.1.

CHEMIST AND BACTERIOLOGIST (male), aged 40-45, wanted by Food Processing Organization in South-West Scotland. Wide experience in food analysis and industrial bacteriology and mycology essential, with special reference to canning of meat products for human and animal consumption and production of protein feeding stuffs. The successful applicant must have a sound theoretical knowledge of human and animal nutrition. He will be required to control research carried out in separate laboratories and to advise management on new techniques. A generous life assurance and pension scheme is in operation, and a car will be provided. Starting salary £2,500.—Requests for application forms to Box 948, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

PHYSICS GRADUATE REQUIRED AS Library Research Assistant for *Encyclopaedia Britannica*. Work: to answer from library sources questions on physics and technical subjects received from subscribers.—Applications (in handwriting), to Mrs. Field, Encyclopaedia Britannica Limited, 67 Great Russell Street, London, W.C.1.

COMMONWEALTH BUREAU OF PASTURES and Field Crops, Hurley, Berkshire, requires Scientific Assistant (abstractor) with degree in agriculture or natural science, and a knowledge of languages. Salary in scale £717 to £1,822. Age, qualifications and experience considered when fixing starting salary. Superannuation.—For further details and application form apply to Director.

LECTURES AND COURSES

BRADFORD INSTITUTE OF TECHNOLOGY

DEPARTMENT OF CHEMICAL ENGINEERING

Short Advanced Course

"WATER USAGE"

Organizing Lecturer: V. C. Marshall, M.I.Chem.E.

Thursday and Friday, March 23 and 24

For details apply to the Registrar, Bradford Institute of Technology, Bradford, 7. (Tel. Bradford 28837).

LANCHESTER COLLEGE OF TECHNOLOGY

COVENTRY

COURSE ON DEVELOPMENTS IN ORGANO-METALLIC CHEMISTRY

A short course will be held on Thursday and Friday, March 16 and 17, 1961. The lecturers will include Dr. J. Chatt (I.C.I. Ltd., Welwyn), Dr. W. Cooper (Dunlop Research Centre), Dr. G. G. Freeman (I.C.I. Ltd., Nobel Division), Dr. W. Gerrard (Northern Polytechnic) and Dr. E. S. Hedges (Tin Research Institute).

Course fee £1 2s. Further details and application forms from the Head of the Chemistry Department.

UNIVERSITY OF LONDON

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

MIDDLESEX HOSPITAL MEDICAL SCHOOL

COURSE FOR M.SC. DEGREE IN RADIATION PHYSICS

An intercollegiate course for this degree will commence in October, 1961, in the above schools of the University. The course, which normally extends over two academic years, will comprise lectures and practical work in nuclear physics and the properties, interactions, applications and hazards of ionizing radiations. (London physics graduates with first- or second-class honours may require only one year.) It is designed as a full-time course for suitable graduates but those working with radiations in medicine and industry may be accepted as part-time students attending not less than six hours per week. The D.S.I.R. has accepted this M.Sc. course as suitable for the tenure of its Advanced Course Studentships. A small number of full-time studentships of £400 per annum plus fees is available for suitably qualified candidates. Fees will be 30 guineas per year.

For further information please apply to Professor J. Rotblat, St. Bartholomew's Hospital, London, E.C.1, or to Professor J. E. Roberts, Middlesex Hospital, London, W.1.

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GRANTS & SCHOLARSHIPS

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

CHEMISTRY DEPARTMENT

A number of bursaries for research in Physical Chemistry will be available in October, 1961, of about equivalent value to D.S.I.R. Research Studentships. Fundamental studies will afford suitable material for submission for a higher degree.

Apply, in writing, giving full academic background and the names of two referees, to Professor R. M. Barrer, F.R.S., Chemistry Department, Imperial College, London, S.W.7.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Bursaries available for postgraduate courses in Aeronautics, Chemical, Civil, Electrical and Mechanical Engineering for Session 1961-62. Value £500 to £700. Applicants should be United Kingdom residents who must have spent at least one year away from university since graduation, preferably in industry.

Further information from the Registrar, Imperial College, London, S.W.7. Closing date May 18, 1961.

THE COUNCIL OF THE ROYAL COLLEGE of Veterinary Surgeons Trust announce the following Scholarship of the Trust: The International League for the Protection of Horses Scholarship for Research in Equine Health Promotion. Value £850 per annum.—Further details from the Secretary, R.C.V.S. Trust, College House, 29-31 Wright's Lane, London, W.8. Closing date for receipt of applications is May 15, 1961.

UNIVERSITY COLLEGE LONDON

Gower Street, W.C.1

DEPARTMENT OF CHEMICAL ENGINEERING

Applications are invited for a Distillers Company Research Studentship, value £450 per annum, plus fees, for work leading to a higher degree on the kinetics of the gaseous oxidation of aromatic hydrocarbons.

Replies to the Secretary at the above address.

NATIONAL COLLEGE FOR HEATING, VENTILATING, REFRIGERATION AND FAN ENGINEERING

NATIONAL COLLEGE ASSOCIATESHIPS

The Governors invite applications from suitably qualified candidates for Scholarships leading to the Associateship of the National College. Applicants will be required to undertake Advanced Studies or Research at the National College in a subject chosen from the following: 1. Heating and Ventilating. 2. Air Conditioning. 3. Fan Engineering. 4. Refrigeration. They should possess one of the qualifications listed below: 1. A degree or equivalent in pure or applied science. 2. A Higher National Certificate in Mechanical Engineering or Applied Physics. 3. A Diploma of the National College plus industrial experience. The value of the awards is £350 per annum plus remission of fees and they are tenable for one year.

Further particulars and form of application may be obtained from: The Clerk to the Governors, at the Borough Polytechnic, Borough Road, London, S.E.1.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for Research Studentships for the Session 1961-62. These studentships of the value of £340 per annum are tenable for one year in the first instance, with possible extension for a second year. Research Studentships may be awarded in any of the following subjects: Mathematics, Physics, Chemistry, Biology, Geology, Communication. Candidates (men or women) should have a good honours degree of a British university but applications from students who expect to graduate in 1961 will also be considered.

Application forms may be obtained from the Registrar, the College, Keele, Staffs, to whom completed forms should be returned not later than May 31, 1961.

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF PHYSICS AND ELECTRONICS

Applications are invited for a Research Studentship supported by the United Kingdom Atomic Energy Authority, for work in an interesting new field of nuclear magnetic resonance in ferromagnetic materials. The research work will be carried out jointly in the Departments of Physics and Electronics. Applicants should have an honours degree in physics or electronic engineering and will be encouraged to submit their work for a higher degree. Tenure is for three years and the salary scale is £600 plus demonstrating fees.

Applications, including full details of qualifications and the names of two referees, should be sent to the Secretary and Registrar, University of Southampton.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

A Research Studentship, of value £450 per annum plus fees and leading to Ph.D., is available for fundamental research in the field of Surface Chemistry.

Applications from prospective graduates in chemistry (or related sciences) should be sent before June 1, to Dr. J. A. Kitchener, Mineral Technology Research Laboratories, Imperial College, London, S.W.7, from whom further particulars may be obtained.

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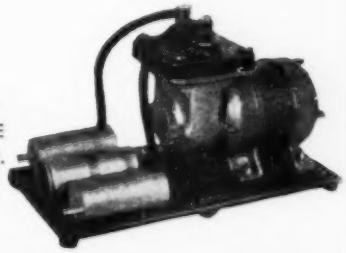

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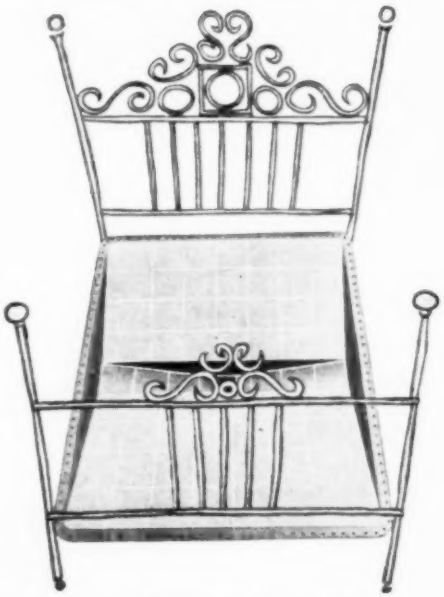

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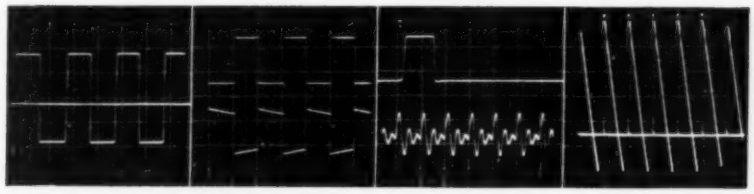

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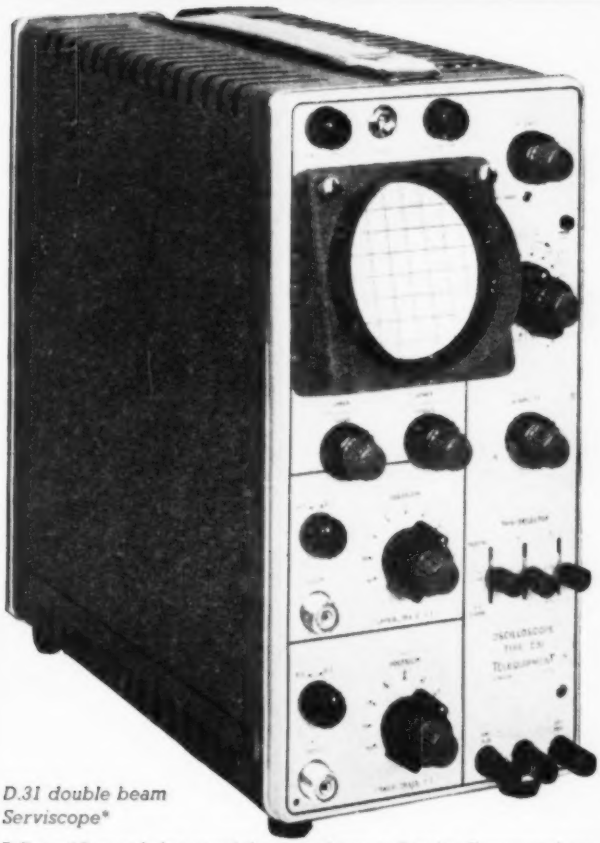

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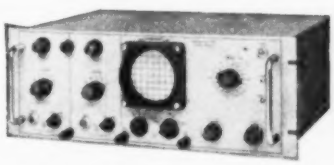

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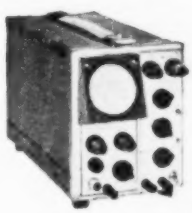

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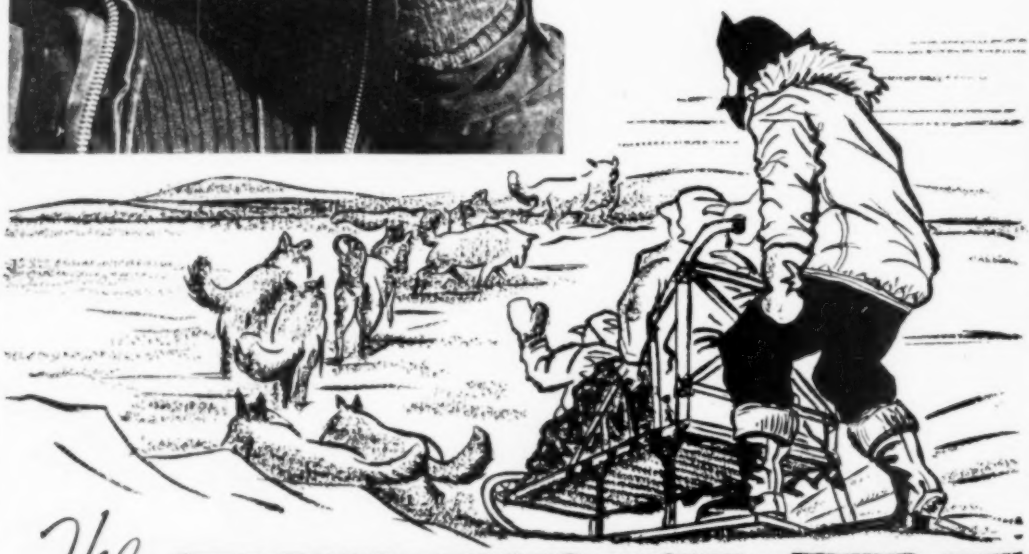

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